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VOL. 15

JANUARY, 1918

No. 1

STUDIES OF ACID PRODUCTION

I. THE VARYING SUSCEPTIBILITY OF CHILDREN TO ACIDOSIS. A PRELIMINARY REPORT *

MARGARET SAWYER, B.Sc., F. A. STEVENS, M.D.

AND

L. BAUMANN, M.D.

IOWA CITY, IOWA

Major and minor surgical operations on children are occasionally followed by an alarming increase in acid production, or acidosis, as it is commonly called. "Periodic vomiting of children," as well as many infectious diseases and disorders of the alimentary canal, is accompanied by an increased acid production. Even a casual survey of the literature leads to the impression that certain children are more susceptible to acidosis than others. The aim of the present work is to determine whether this individual susceptibility can be demonstrated experimentally.

METHODS

Apparently healthy male children between the ages of 4 and 8 years were placed in a metabolism ward under the supervision of a special nurse. The diets were prepared by a special dietitian. The urine at each voiding was separately collected in a jar and its approximate volume noted. It was preserved in a refrigerator after the addition of toluene. The next morning the twenty-four-hour volume was accurately measured and checked with the nurse's record. A creatin-free diet containing about 55 calories per kilogram was administered during the normal periods. Protein constituted 25, fat 30, and carbohydrate 45 per cent. of the total calory intake. The nitrogen intake was approximately constant throughout the normal and high fat periods. After the excretion of acid, ammonia and creatinin had become practically constant, the intake of each of the three classes of foodstuffs was reduced to one third. When distinct signs of acidosis appeared, the normal diet was resumed and continued until the excretion of acid and

* Submitted for publication Oct. 16, 1917.

* From the Departments of Home Economics and Internal Medicine, State University of Iowa.

ammonia had approximately attained their former level, when the fourth period was begun. During this period the protein intake remained the same as in the normal period, the carbohydrate was reduced to about 6 per cent., while fat rose to about 68 per cent. of the total calory intake. The normal diet was resumed when signs of acidosis appeared. The total nitrogen, ammonia, titratable acid,¹ creatinin² and creatin of the urine were quantitated each day. In a few instances the acetone bodies (acetone, acetic acid and oxybutyric acid in terms of acetone) and phosphorus of the urine were estimated as well. Qualitative tests for acetone, sugar and albumin were carried out in routine fashion each day. The carbon dioxid combining power of the plasma was determined according to the method of Van Slyke³ before breakfast, during the normal, low calory and high fat periods. In quite a few instances the acetone bodies, and in several, the calcium, glucose and fat content of the blood, were studied.

The acid equivalent of the food was computed from Sherman and Gettler's valuable tables.⁴ The acetone bodies of the blood were determined according to Marriott,⁵ glucose according to Lewis and Benedict,⁶ calcium according to the micromethod of Marriott,⁷ and fat according to the nephelometric method of Bloor.⁸

EXPERIMENTS

The present report includes observations on ten boys. The results are tabulated. Cases 5, 8 and 6, illustrating a severe, a moderate and a slight reaction, have been graphically represented (Charts 1, 2 and 3). In the tables the titratable acid and ammonia are expressed in terms of tenth-normal solution. According to Henderson and Palmer¹ these values are "strictly additive." The values for acetone and oxybutyric acid of the blood, which appear in the chart, are expressed in terms of milligrams per cent.

CASE 1.—C. C., aged 5 years; weighed 17 kg.; physical examination was negative, except for a discharging sinus from an old osteomyelitis.

1. Henderson, L. J.: *Jour. Biol. Chem.*, 1911, **9**, 403.

2. In the presence of acetone creatinin was determined according to the method of G. Graham and E. P. Poulton, *Proc. Roy. Soc., Series B*, 1913-1914, **87**, 205.

3. Van Slyke, Donald D.: *Jour. Biol. Chem.*, 1917, **30**, 347.

4. Sherman, H. C., and Gettler, A. O.: *Jour. Biol. Chem.*, 1912, **11**, 323.

5. Marriott, W. McK.: *Jour. Biol. Chem.*, 1914, **18**, 507.

6. Myers, V. C., and Bailey, C. V.: *Jour. Biol. Chem.*, 1916, **24**, 147.

7. Marriott, W. McK.: Private communication. We are indebted to Dr. Marriott for this courtesy.

8. Bloor, W. R.: *Jour. Biol. Chem.*, 1914, **17**, 377.

TABLE 1.—DATA FROM CASE 1

Day	Ti- tra- table Acid, C.c.	Am- monia, C.c.	Creat- inin, Mg.	Crea- tin, Mg.	Acetone Quali- tative	Nitro- gen in Urine, Gm.	P ₂ O ₅ in Urine, Gm.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.	Acetone Bodies in Blood, Mg., per Cent.
1	—9*	226	211	51		9.1	0.85			
2	48	291	219	36		6.2	0.93			
3	94	338	223	37		9.8	1.43			
4	139	276	206	56		7.6	1.06			
5	86	270	213	57		8.0	1.0			
6	71	303	222	64		8.3	0.92			
7†	110	307	200	120	+	9.8	1.93	52	100	5.1
8†	161	622	196	102	+++	10.8	1.86			
9	70	773	198	97	++	9.6	1.12	21	50	30.0
10	36	446	222	13	+	6.6	0.46			
11	26	360	210	15		5.1	0.43			
12‡	54	192	194	32	+	6.5	0.82			
13‡	100	213	187	95	+	6.3	1.32	49	90	12.0
14	90	355	193	122	++	6.9	0.90			
15	41	366	230	7		6.3	0.52			
16	53	357	207	9		6.3	0.47			
17	43	316	200	22		6.6	0.63			

* Alkaline urine.

† High fat diet.

‡ Low calory diet.

REMARKS: On the second day 300 c.c. of tenth-normal phosphoric acid solution (neutral red was employed as the indicator) was administered per os. This was followed by a prompt rise of the titratable acid and ammonia excretion, but by no subjective or objective symptoms. After twenty-four hours on the high fat diet the child complained of nausea. Some irregularity of the pulse was noted on the following day. Slight irregularity of the pulse was present after thirty-six hours on the low calory diet. The next morning the face was slightly flushed. During the period of high fat feeding the sinus discharged more freely than during the low calory period.

The response to the high fat diet was rapid and marked.

CASE 2.—C. G., aged 5 years; weighed 23 kg. Physical examination was negative.

TABLE 2.—DATA FROM CASE 2

Day	Titratable Acid, C.c.	Ammonia, C.c.	Creatinin, Mg.	Creatin, Mg.	Acetone, Qualitative	CO ₂ Com- bining Power
1	125	385	276	192		
2	185	385	274	194		
3	120	395	274	174		50
4*	140	330	272	178	+	
5*	170	500	256	236	++	
6*	240	815	244	290	+++	29
7	...	818	234	202		

* High fat diet.

REMARKS: The metabolism of this child (Case 2) was studied for another purpose and will be reported in detail in a subsequent paper. During the period of high fat feeding a slightly increased pulse rate and some restlessness were manifest.

CASE 3.—H. G., a nervous child with a neuropathic family history and marked chronic tonsillitis. The Wassermann reaction was one plus. The child was aged 8 years and weighed 17 kg.

TABLE 3.—DATA FROM CASE 3

Day	Titra- table Acid, C.e.	Am- monia, C.e.	Oreat- inin, Mg.	Orea- tin, Mg.	Nitrogen in Urine, Gm.	Ac- etone in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Ca in Blood, Mg., per Cent.	Fat in Blood, Mg., per Cent.	Glucose in Blood, Mg., per Cent.
1	100	189	292	248	8.1					
2	81	225	264	241	8.5	0.4	51	13	670	50
3*	99	206	284	277	8.4					
4*	182	316	288	272	6.7					
5*	175	619	284	233	7.9	24.0	32	15	1,330	20
6	60	602	249	189	8.6					
7	30	898	250	95	7.5					
8	10	228	231	112	8.0					
9	10	189	271	181	9.6					
10	78	230	260	166	7.5					
11	13	328	284	231	9.8					
12†	112	227	271	176	10.1					
13†	96	476	260	238	11.2					
14	69	580	253	133	9.5	4.3	35	13	660	60
15	55	484	277	61	8.3					
16	65	233	249	48	7.2					
17	82	247	263	71	7.7					

* Low calory diet.

† High fat diet.

REMARKS: The urine was collected in twelve-hour periods. The creatin output during the day was always considerably higher than at night. This is in agreement with the observation of Powis and Raper.⁹ After the boy had been on the low calory diet for twenty-one hours he complained of nausea, and later, vomited. Nineteen hours later the pulse became intermittent and weaker. When the normal diet was resumed the child became comfortable in a remarkably short time.

After thirty-six hours on the high fat diet the patient became somewhat drowsy and the pulse became slower.

On the whole this child reacted very promptly. The low sugar value of the blood is significant.

Meat was fed during the first five days of the experiment.

This child responded to both diets fairly rapidly.

9. Powis, F., and Raper, H. S.: *Biochem. Jour.*, 1916, **10**, 363.

CASE 4.—T. H., aged 6 years; weighed 18.3 kg. Physical examination was negative.

TABLE 4.—DATA FROM CASE 4

Day	Titra- table Acid, C.c.	Am- monia, C.c.	Creat- inin, Mg.	Creatin, Mg.	Nitrogen in Urine, Gm.	P ₂ O ₅ in Urine, Gm.	Acetone Bodies in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.
1	86	302	281	72	8.5	2.02			
2	120	240	264	61	8.3	1.29	3.2	67	78
3*	123	282	264	100	10.0	1.54			
4	133	580	253	113	11.5	1.75	19.0	35	88
5	62	449	271	24	9.4	0.90			
6	8	381	248	89	8.5	1.05			
7	50	297	251	72	9.0	1.26			
8	42	239	253	80	8.8	1.24			
9†	82	197	254	86	6.2	0.98			
10†	86	210	269	115	7.0	1.40			
11	69	361	233	124	9.8	1.42	22.0	31	74
12	22	384	234	21	8.6	1.02			
13	29	336	243	21	7.7	0.99			
14	56	302	254	33	8.1	1.03			
15	34	287	253	61	8.6	1.38			
16	90	276	239	39	8.9	1.88			

* High fat diet.

† Low calory diet.

REMARKS: After twenty hours on the diet of high fat the patient reacted with vomiting; the pulse and respirations were slightly increased. During the experiment the patient had an acute rhinitis.

The response to the high fat diet was rapid in this case.

CASE 5.—C. H., aged 8 years; weighed 20.9 kg. Physical examination showed atrophy and paralysis of both legs following anterior poliomyelitis, chronic tonsillitis of medium grade, and adenoids. The child was also mentally deficient.

TABLE 5.—DATA FROM CASE 5*

Day	Titra- table Acid, C.c.	Am. monia, C.c.	Creat- inin, Mg.	Creatin, Mg.	Nitrogen in Urine, Gm.	P ₂ O ₅ in Urine, Gm.	Acetone Bodies in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.
1	45	281	182	67	6.5	1.22			
2	72	356	167	54	4.9	1.15			
3†	90	323	144	107	5.6	1.08	8.0	58	70
4†	160	579	160	200	7.4	1.37			
5	71	755	142	190	7.7	1.23	50.0	31	
6	47	663	159	64	5.3	0.49			
7	54	395	164	58	5.9	0.41			
8	56	346	172	136	7.5	0.52			
9	45	273	144	153	6.9	0.73			
10†	87	242	146	173	8.0	1.27			
11†	142	598	144	214	10.2	1.86	30.0	20	40
12	70	763	151	117	5.5				
13	30	632	152	44	6.6				
14	40	543	153	34	6.5				
15	52	443	157	52	6.4				
16	62	323	156	36	6.3				
17	90	320	156	73	6.6				
18	67	314	160	100	6.6				

* Refer to Chart 1.

† Low calory diet.

‡ High fat diet.

REMARKS: On the low calory diet the boy's pulse became irregular in twelve hours and markedly so in thirty-six hours. At the end of forty hours emesis and dizziness were observed. Drowsiness set in at the end of forty-eight hours. After twelve hours on the high fat diet the face was slightly flushed. After twenty-four hours some vertigo was observed.

It was subsequently ascertained that this child developed a severe acidosis following the simple operation of section of the Achilles tendon.

The reaction to both diets was rapid and large.

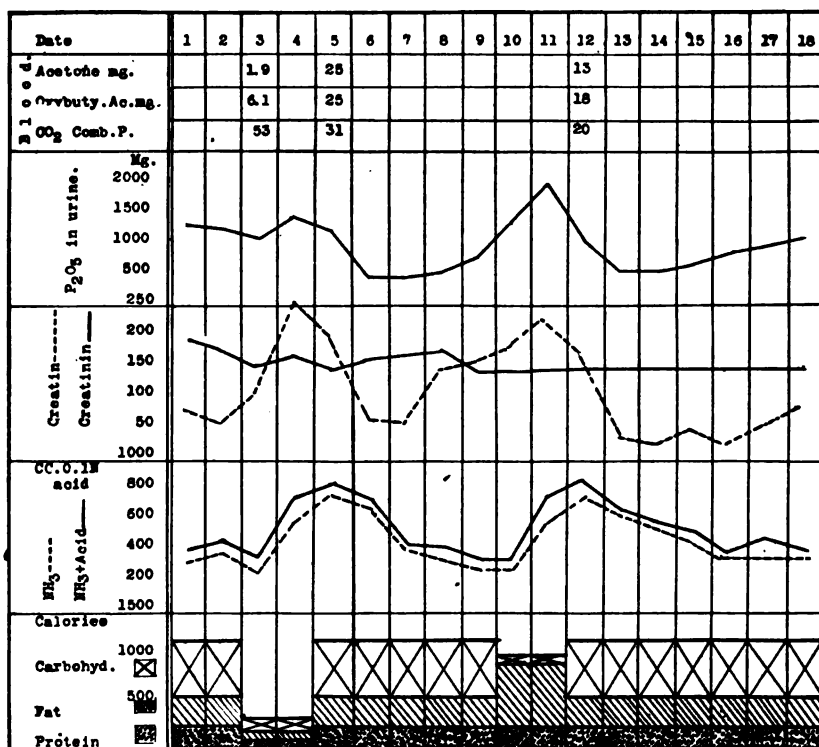


Chart 1.—Case 5. Severe acidosis.

CASE 6.—J. H., aged 5 years; weighed 20.5 kg. Physical examination showed enlarged tonsils filling half the lumen of the pharynx, and mental deficiency.

TABLE 6.—DATA FROM CASE 6*

Day	Titra- table Acid, O.c.	Am. monia, O.c.	Creat- inin, Mg.	Crea- tin, Mg.	Nitrogen in Urine, Gm.	Ac- etone Bodies in Blood, Mg., per Cent.	OO ₂ Com- bining Power	Calcium in Serum, Mg., per Cent.	Glucose in Blood, Mg., per Cent.	Fat in Blood, Mg., per Cent.
1	88	376	386	184	9.2					
2	80	309	332	141	9.1					
3†	94	304	374	171	8.9	4.7	56	12	87	660
4†	119	270	332	278	8.3					
5†	112	227	316	306	7.6					
6†	86	329	282	261	7.2					
7†	87	266	278	226	6.0					
8†	75	312	216	201	6.4					
9†	62	284	235	191	5.0					
10	—15†	275	293	190	8.2					
11	0	315	347	49	8.3	14.0	57	14	74	450
12	20	285	327	26	8.8					

* Refer to Chart 2.

† Low calory diet.

‡ Urine was alkaline.

REMARKS: After forty hours on the low calory diet there was no evidence of acidosis except an irregular pulse, and no evidence of acidosis four days later. On the eleventh day the boy developed elevation of temperature (104 F.) coincident with a rise in the creatinin output. Later a typical measles rash developed.

This boy responded very little, if at all, after seven days on the low calory diet.

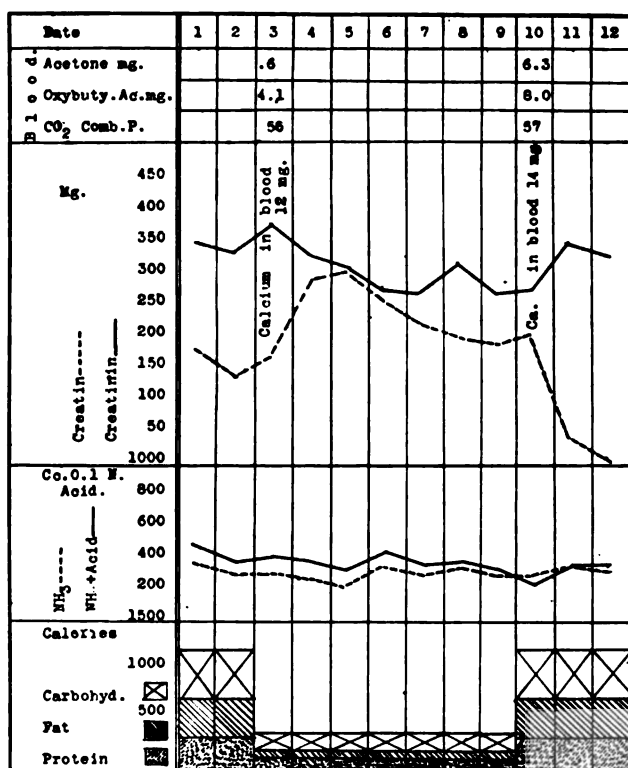


Chart 2.—Case 6. Little or no acidosis.

CASE 7.—T. K., aged 5 years; weighed 14.1 kg. Physical examination showed paralysis of both legs, due to anterior poliomyelitis, and slight cervical adenitis, but no evidence of the lymphatic state.

TABLE 7.—DATA FROM CASE 7

Day	Ti- tra- table Acid, C.c.	Am- monia, C.c.	Oreat- inin, Mg.	Orea- tin, Mg.	Nitro- gen in Urine, Gm.	P ₂ O ₅ in Urine, Gm.	Acce- tone Bodies in Urine, Mg.	Acce- tone Bodies in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.
1	61	200	187	132	7.4					
2	50	239	190	108	7.9					
3	77	247	179	82	6.3		570	...	50	104
4	67	238	179	136	7.0		450			
5*	56	223	188	156	7.5		371			
6*	82	301	151	206	5.5		645			
7*	88	416	151	112	4.7	0.96	727			
8	46	347	157	88	6.6	0.70	191	27	41	54
9	15	254	164	26	5.6	0.77	112			
10	—10†	247	135	22	5.9	0.82	52			
11‡	58	212	155	47	7.0		68			
12‡	112	322	158	146	8.2		129			
13‡	110	543	144	159	8.4	1.16	588			
14	73	417	131	89	7.4	1.24	133	25	40	
15	32	322	130	47	7.9	0.98				
16	—31†	223	131	34	6.4	0.94				
17	0	227	142	39	6.7	1.06				

* Low calory diet.

† Urine alkaline.

‡ High fat diet.

REMARKS: The combined sulphur and phosphorus content of the diet during the period of high fat feeding was equivalent to 400 c.c. of tenth-normal acid. During the period of low calory feeding no symptoms of acidosis were observed; during the period of high fat feeding slight drowsiness was noted, but no other symptoms.

The responses to the diet in this case were relatively slight.

CASE 8.—C. W., aged 8 years; weighed 22.2 kg. Physical examination showed paralysis of both legs due to anterior poliomyelitis and mild chronic tonsillitis.

TABLE 8.—DATA FROM CASE 8*

Day	Titra- table Acid, C.c.	Am- monia, C.c.	Creat- inin, Mg.	Crea- tin, Mg.	Nitrogen in Urine, Gm.	Ac- etone Bodies in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.	Fat in Blood, Mg., per Cent.	Calcium in Serum, Mg., per Cent.
1	81	291	800	235	7.9					
2	78	398	809	275	9.3					
3†	74	259	259	252	6.8	6.5	69	84	870	12
4†	120	212	278	375	6.8					
5†	180	278	270	261	6.6					
6†	180	432	276	192	5.8					
7†	86	437	286	146	5.1					
8	61	520	262	196	6.4	21.0	46	96	880	14
9	-15‡	306	276	123	6.8					
10	-15‡	240	274	196	7.9					
11	21	301	290	256	8.5					
12§	110	265	261	456	9.5					
13§	162	450	254	363	11.2					
14§	193	693	248	479	12.2					
15§	40	776	240	328	11.8		49	90	890	16
16	122	703	277	283	10.1					
17	14	498	270	227	9.1					
18	67	411	258	272	8.6					

* Refer to Chart 3.

† Low calory diet.

‡ Alkaline urine.

§ High fat diet.

REMARKS: No symptoms were observed during the period of low calory diet. Sixty hours after beginning high fat diet the child complained of drowsiness.

Our impression is that the responses of this case to the diets were normal for a child of 8 years.

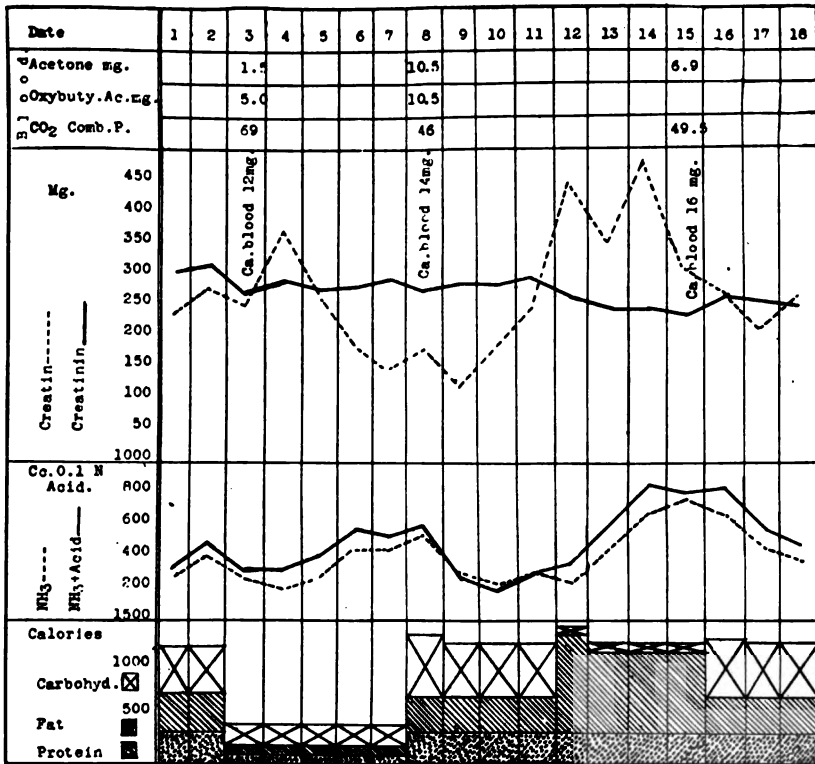


Chart 3.—Case 8. Moderate acidosis.

CASE 9.—R. W., aged 8 years; weighed 23.2 kg. Physical examination showed scar of mastoid operation, and that the tonsils had been removed.

TABLE 9.—DATA FROM CASE 9

Day	Titratable Acid, C.c.	Ammonia, C.c.	Creatinin, Mg.	Creatin, Mg.	Acetone, Qualitative	CO ₂ Com- bining Power
1	100	465	332	96		
2	110	455	362	86		
3	100	465	336	143		49
4*	120	390	362	124	+	
5*	120	425	342	216	++	
6*	145	530	384	250	+++	37
7	...	630	361	297		

* High fat diet.

Further studies carried out on Case 9 will be reported in a subsequent paper.

CASE 10.—B. W., aged 4 years; weighed 13.4 kg. Physical examination showed severe chronic tonsillitis with marked cervical adenitis, recent anterior poliomyelitis and a nervous temperament.

TABLE 10.—DATA FROM CASE 10

Day	Ti- tra- table Acid, O.c.	Am- monia, O.c.	Creat- inin, Mg.	Crea- tin, Mg.	Nitro- gen in Urine, Gm.	P ₂ O ₅ in Urine, Gm.	Ac- tone Bodies in Urine, Mg.	Ac- tone Bodies in Blood, Mg., per Cent.	CO ₂ Com- bining Power	Glucose in Blood, Mg., per Cent.
1	98	264	192	118	8.9	1.24				
2	96	228	218	147	7.5	1.32				
3	78	257	184	81	7.2	1.07	78			
4*	148	250	192	152	9.0	1.80	116	3.1	50	102
5	116	296	178	93	7.2	1.38	...	11.0	37	55
6	70	390	188	91	6.8	0.90				
7	37	218	169	86	6.8	0.97				
8	68	242	174	81	7.2	1.13	96			
9	55	219	185	68	7.6	1.18				
10†	89	169	182	116	5.8	1.13	215			
11†	92	199	171	139	5.5	1.23	446	16.0	39	66
12	47	337	156	121	7.1	0.74	120			
13	48	341	180	37	6.8	0.71	78			
14	57	297	156	54	6.0	0.71				
15	45	264	161	78	6.8	1.01				
16	54	255	178	67	6.9	1.03				

* High fat diet.

† Low calory diet.

REMARKS: This child became restless and drowsy after twenty-four hours on the low calory diet. Twenty-four hours later the pulse became slow and irregular. Twenty hours after beginning the high fat diet vomiting occurred.

Although this child developed symptoms of acidosis very rapidly, the urine and blood analyses revealed only moderate changes.

TABLE 11.—SUMMARY OF DATA FROM PREVIOUSLY REPORTED CASES

Subject	Age, Years	Normal Period, Plasma Carbonate	Normal Period, Acetone Bodies* in Blood, Mg., per Cent.	Low Calory Period, Plasma Carbonate	Low Calory Period, Acetone Bodies* in Blood, Mg., per Cent.	High Fat Period, Plasma Carbonate	High Fat Period, Acetone Bodies* in Blood, Mg., per Cent.
T. H.	6	67	3.2	35 (2)	18.7	31 (1)	22
O. O.	5	52	5.1	48 (2)	12.2	21 (2)	30
T. K.	5	50	0.0	41 (3)	27	40 (2)	25
O. H.	8	53	8.0	31 (4)	50	20 (2)	30
H. G.	8	50	...	32 (3)		35 (2)	
J. H.	5	56	4.7	57 (7)	14		
O. W.	8	69	6.5	46 (5)	21	49 (4)	
B. W.	4	50	3.1	39 (2)	16	37 (1)	11
R. W.	6	51	...			37 (1)	
C. G.	5	50	...			29 (3)	
R. W.	8	49	...			37 (3)	
L. S.	7	56	...		...	30 (1)	
Average	...	54					

* Acetone bodies include acetone, aceto-acetic and oxybutyric acids (in terms of acetone). The numerals in parentheses refer to the number of days preceding the determination during which the child received the acid-producing diet.

DISCUSSION

A difference in reaction towards the acid-producing diets is apparent from the blood and urine analyses and also in the time which elapsed before a marked response occurred. The cause of this variation is at present more or less conjectural. Thus far we have not been in a position to associate it with a particular state or condition of the subject. All the children had been on similar hospital diets for months preceding this investigation. The response to the high fat diet was apparently more rapid and greater than to the low calory diet.

In a recent publication, Jeans and Johnston¹⁰ observe that starvation does not always produce a marked increase of the acetone bodies in the blood of children. They refer to a patient who after a fast of five days showed 6.6 mg. per cent. of acetone bodies and 50.5 volume per cent. of plasma carbonate. At the end of eight days 22.6 mg. per cent. of acetone bodies and 56 volume per cent. of carbonates were present in the blood. This observation is quite similar to our own on Case 6 (Chart 1). On the other hand, we have found, in several instances,

10. Jeans, P. C., and Johnston, M. R.: AM. JOUR. DIS. CHILD., 1917, **14**, 57.

that noteworthy symptoms of acidosis may appear in less than twenty-four hours on the low calory diet. The symptoms most often encountered were nausea, vomiting, drowsiness, irregularity and slowness of the pulse and increase in the number of respirations.

The titratable acid of the urine, which is largely due to a preponderance of acid phosphate, increases as the result of change in the diet, before the ammonia.¹¹ This increase is accompanied by an absolute increase in the phosphate of the urine, without a compensatory decrease in the fecal output, as will be shown in a future publication.¹² The increased acid elimination is often followed by a period of diminished excretion and this is paralleled by the phosphate excretion.

The increase in the ammonia excretion becomes apparent, usually on the second day following the ingestion of the acid-producing diet and is prolonged for several days after the resumption of the normal diet. This observation is in agreement with that of Veeder and Johnston.¹³

Creatinin was practically constant throughout for each individual. As pointed out by Folin and others, it may be considered a constant and an indicator of the accuracy with which the urine has been collected. Creatin is uniformly increased during the periods of increased acid production. This increase is not attributable, apparently, to the acid condition per se¹⁴ (Chart 2). The period of increase is often followed by one of markedly diminished excretion, occasionally lasting several days.

While the nitrogen excretion varied within rather wide limits, an unmistakable rise during the period of high fat feeding was present. This increase is uniformly accompanied by an increased creatin excretion and may be due to muscle breakdown. During the low calory period twice the amount of nitrogen ingested was eliminated through the urine. The increased elimination during the acid periods was occasionally followed by retention.

Qualitative tests for the presence of aceto-acetic acid in the urine were carried out daily by means of the Rothera modification of the Legal test. In some instances the urine of each voiding, following the administration of the acid-producing diets, was tested separately. We

11. Sellards, A. W.: *Bull. Johns Hopkins Hosp.*, 1912, **23**, 289.

12. Fitz, R., Alsberg, C. L., and Henderson, L. J.: *Am. Jour. Physiol.*, 1907, **23**, 113. These authors found an increase of phosphorus in the urine of rabbits fed with hydrochloric acid. See also Steenbock, H., Nelson, V. E., and Hart, E. B.: *Jour. Biol. Chem.*, 1914, **19**, 399.

13. Veeder, B. S., and Johnston, M. R.: *Am. Jour. Dis. Child.*, 1917, **13**, 89.

14. The administration of hydrochloric or sulphuric acid to children may be followed by a rise in the excretion of ammonia and titratable acid in the urine without a rise in creatin (unpublished observations).

were occasionally surprised at the rapidity of the response. In two instances the high fat diet was instituted at 7:30 a. m. and a trace of aceto-acetic acid was found in the urine passed four hours later. Veeder and Johnston found that one-half of their patients (many of whom were infants), when deprived of nourishment, did not show an increase in the acetone bodies during the first twenty-four hours, but all responded during the second day of the fast. Their Case 16, however, responded very feebly with acetone and not at all with increased ammonia excretion.

Throughout these experiments we have obtained the impression that the carbonate values of the plasma are a reliable index of the severity of the acidosis. In one case (Case 6, Chart 2) we found an increase of the acetone bodies of the blood, with a normal carbonate value. While we have not determined the coefficient used by Fitz and Van Slyke,¹⁵ the tables show that in a general way the combining power appears to be inversely proportional to the sum of the ammonia and titratable acid. The average normal plasma carbonate value for 12 children between the ages of 4 and 8 years was 54 volume per cent. (Table 11).

In a general way the increase of acetone bodies in the blood was proportionate to the severity of the acidosis. The glucose content of the blood was examined in eight cases; of these, six showed a decrease during the period of acidosis; two did not. Though this observation is suggestive, it should be confirmed on a larger series of cases. For want of blood we were unable to determine the calcium content of the serum in more than three cases. All showed an increase during the periods of increased acid production.

SUMMARY AND CONCLUSIONS

The reaction of ten children to acid-producing diets was studied.

Tables and charts recording the results of the blood and urine analyses have been made.

A careful survey of the tables and charts leads to the conclusion that the response to an acid-producing diet is a variable factor among the different children examined.

We desire to express our indebtedness to Prof. L. W. Dean for suggesting the problem and for his cooperation; to Prof. A. Steindler and Prof. A. H. Beifeld for their cooperation, and to Miss Helen Mougey for the care exercised in the preparation of the diets.

The research was made possible by a grant from the funds of the Graduate College of the State University of Iowa.

15. Fitz, R., and Van Slyke, D. D.: *Jour. Biol. Chem.*, 1917, **30**, 389.

THE INTRAPERITONEAL INJECTION OF SALINE SOLUTION *

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AND

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BALTIMORE

The parenteral administration of water is a widely used therapeutic measure in the treatment of the severe nutritional disorders of infants, especially when, after continued vomiting and diarrhea, marked loss of body fluids has resulted. It is an efficacious means of combating this serious complication.

Without entering into a discussion as to the relative merits of the procedures used to introduce water, it may be said that the methods which have been employed leave much to be desired. The vomiting and diarrhea are usually so severe in the cases that require water that they prevent its administration by mouth or rectum. Intravenous injection is often difficult, and it is rarely possible to inject an amount sufficient for the purpose without throwing too great a burden on the circulation. The subcutaneous method is the one on which chief reliance has been placed. In our hands the results from this method have been disappointing. Absorption from the subcutaneous tissues is often very slow and after repeated injections is almost nil.

An efficient method for the administration of water for therapeutic purposes must fulfil several important requirements: (1) It must admit of the administration of comparatively large amounts at one time and permit of repetition at frequent intervals; (2) the water must be quickly absorbed; (3) the method must be simple of procedure, practicable and accompanied by a minimum of risk to the patient.

We believe that the injection of water¹ directly into the peritoneal cavity fulfils all of these requirements. This method is not original with us. We have employed it at the suggestion of Dr. Howland who saw it used as a routine measure on the service of Professor Garrod at St. Bartholomew's Hospital, London. No reference to this method has been found in the literature. It has been used extensively in the

* Submitted for publication Oct. 27, 1917.

¹ From the Department of Pediatrics, The Johns Hopkins University, and The Harriet Lane Home, The Johns Hopkins Hospital.

1. By water we mean physiologic sodium chlorid solution; the water is the essential element, and we believe that physiologic sodium chlorid solution is as effective as any of the other solutions which are recommended. It may be that as more information regarding the loss of salts in diarrheal conditions is obtained, a solution better meeting the requirements may be found.

Harriet Lane Home, The Johns Hopkins Hospital, for the past two years and with such satisfactory results that we consider it a distinct improvement on any of the other methods that we have used.

The amount of water that can be given depends on the size of the patient. In small infants 100 to 250 c.c. may be introduced and the injection can be repeated every twelve to twenty-four hours. In larger infants a greater amount (300 to 400 c.c.) may be given at one time. We have observed no untoward effects from the injection of such amounts, even when they have been frequently repeated.

The rapidity of the absorption of fluid from the peritoneal cavity is shown by the experiments of Dandy and Rowntree.² They found that 40 to 60 per cent. of phenolsulphonephthalein in solution was absorbed in one hour. The absorption took place directly into the blood stream and was not influenced by posture. Clinical evidence of its rapid absorption in patients we have treated is shown by the fact that the distention of the abdomen which usually follows the introduction of water intraperitoneally subsides after a short time. In a moribund patient 200 c.c. of normal saline solution were injected and the patient died six hours later. At the necropsy, which was performed immediately, less than 50 c.c. of the solution were recovered.

When this method is used great care in technic should be exercised. After considerable experience in the wards, however, controlling the method with animal experiments and with the findings at necropsy, we have become convinced that the attendant dangers are minimal. We have never seen any complications follow its use.

The following protocols are given to illustrate the effect of the injection of physiologic sodium chlorid solution into the peritoneal cavity of rabbits.

PROTOCOLS

ANIMAL 120.—Weight, 1,500 gm., injected with 50 c.c. physiologic sodium chlorid solution; killed three hours after injection. Necropsy findings: Hemorrhage (3 by 4 cm.) in the abdominal wall at site of injection, and slight edema of the subcutaneous tissues; injection of the vessels supplying this region. Point of entrance into peritoneum clean. Intestines show no abrasions. About 20 c.c. of slightly turbid fluid free in peritoneal cavity, with no large flakes of fibrin. Smears from fluid in peritoneal cavity showed a few polymorphonuclear cells, but no organisms. The cultures were sterile.

ANIMAL 117.—Weight, 1,600 gm.; injected with 50 c.c. normal saline solution, killed two and a half days after injection. Necropsy findings: Remains of slight hemorrhage in abdominal wall at site of injection. Point of entrance into peritoneal cavity not visible. Intestines everywhere smooth and glistening. No free fluid. No adhesions. Two or three flakes of fibrin found. Smears made from the flakes of fibrin show a few leukocytes, but no organisms. The cultures were sterile.

2. Dandy and Rowntree: *Ann. Surg.*, 1914, **59**, 587.

The following is the report by Dr. A. H. Clark of the necropsy on a patient who was treated with intraperitoneal injections of physiologic sodium chlorid solution. The patient was a colored infant weighing 20 pounds, which was brought to the hospital with vomiting, diarrhea and acidosis and died thirty-six hours later. The infant received two intraperitoneal injections of physiologic sodium chlorid solution, one of 250 c.c. eighteen hours before death, and one of 200 c.c. six hours before death.

The abdomen is moderately distended and is symmetrical. At a point slightly below the umbilicus are two small fresh puncture wounds. On opening the peritoneal cavity the abdominal wall shows a slight extravasation of blood below these wounds, but there is no apparent abrasion of the peritoneal surface. Neither on the skin nor in the abdominal wall is there any evidence of an inflammatory reaction around these wounds. The peritoneal cavity contains about 20 c.c. of clear yellow fluid. The peritoneal surfaces are smooth and glistening and there are no localized areas of peritoneal roughening. The viscera are normally disposed and are not adherent. The intestines below the site of puncture show no abrasions.

The procedure must be carried out with strict aseptic precautions. It is not to be attempted where there is marked abdominal distention, at least not until this has been relieved, and care should be exercised that the bladder is not distended. Objection to the method may be raised because of the danger of puncturing the intestine during the introduction of the needle and from this same danger while the fluid is being introduced. This has not occurred in our series of cases.

TECHNIC

The technic is as follows: The patient lies in the recumbent posture with the movements of arms and legs restricted by a restraining jacket. The most favorable site for the introduction of the needle is through the linea alba just below the umbilicus. The skin is prepared after the usual surgical method, with iodine and alcohol, and the area may be rendered anesthetic with ethyl chlorid. The solution³ is introduced by gravity from an infusion bottle. When the patient is restrained in the proper position and the site for the injection prepared, the skin and subcutaneous tissues are picked up between the thumb and the index finger and the needle,⁴ pointing upward, is inserted at an oblique angle. After it has penetrated the peritoneum the fluid is allowed to flow into the peritoneal cavity.

The injection of the fluid is continued until the abdomen becomes slightly distended. It should not be introduced too rapidly or in too large quantities, to avoid the possibility of embarrassing the respiratory and circulatory systems. One hundred to 250 c.c. can be introduced in from fifteen to twenty minutes. The fluid flows in so rapidly that the solution does not become cooled below that of the body temperature. After the fluid has been introduced, the needle is withdrawn and the puncture wound covered with a sterile dressing. The

3. The solution which we have used is the so-called "normal saline solution" (0.8 per cent. sodium chlorid). This is made with freshly distilled water and promptly sterilized. It is injected at a temperature of 100 F.

4. We use an 18-gage nickeloïd needle, 2 inches long, and the rubber tubing is fastened to the hub of the needle.

injection may be repeated after twelve to twenty-four hours, if necessary. The injection may be made, if desired, outside of the left rectus muscle about half way between the costal margin and the left anterior superior spine of the ileum.

The beneficial effects are first apparent in the general appearance of the patient. The feeble whine is often replaced by a stronger, more vigorous cry. The extreme restlessness lessens and thereafter the child frequently sleeps in a normal manner. The tongue, lips and the skin become moist, the fontanel is less depressed and the gray cyanosis or pallor disappears. The most striking change is the alteration in the facial expression. The eyes are less sunken and the anxious, painful expression is often lost. In a number of instances we have observed a very marked increase in the pulse rate and in the secretion of urine. The improvement is often so marked that only one injection has been necessary in patients who were in an apparently hopeless condition on admission. Occasionally a febrile reaction follows the introduction of the fluid. The temperature may range from 100 to 103 F., but it usually subsides after twelve to forty-eight hours. After the introduction of water the weight in some patients remains stationary, while in others there may be a gain in weight. After repeated injections there may be edema. A marked increase in weight is rarely permanent, but even with the loss of weight in such instances the improved general condition of the patient is maintained.

The results have been so encouraging that we have adopted this method in the treatment of all cases of severe gastro-intestinal disturbance when the introduction of water in sufficient quantity by mouth is impossible. If the condition of the patient demands it the intraperitoneal injection is made immediately on admission to the hospital. The indications for repeating the intraperitoneal injection are, the general condition of the patient and continuation of vomiting. When the vomiting has ceased water is given by mouth, and as early as possible thereafter the food which is indicated is begun. In patients with acidosis, alkaline therapy as recommended by Howland and Marriott⁵ is used.

We do not wish to give the impression that the intraperitoneal route is to be used to the exclusion of the other prescribed methods for introducing water. Each serves its purpose. We do, however, recommend its use in cases in which the introduction of water as a therapeutic agent is urgently demanded.

While the case reports which are appended illustrate only the benefits resulting from the use of this method in the severe nutritional disturbances of infancy with and without acidosis, its usefulness may be extended to many other conditions in which the parenteral administration of water is indicated.

5. Howland and Marriott: *Bull. Johns Hopkins Hosp.*, 1916, **27**, 63.

REPORT OF CASES

CASE 1.—M. H., aged 5 months; weight, 8 pounds.

The patient gained on woman's milk until 3½ months old, when it became necessary to feed her artificially. On a proprietary food the weight increased for a short time, then it became stationary, and finally, with the development of loose stools, fell rapidly. She was admitted to the hospital in a state of collapse, with gray color, sunken eyes, dry lips, weak cry, subnormal temperature and weak pulse. She vomited and had thirteen loose green stools in the first twenty-four hours in the hospital. There was no hyperpnea. The leukocytes were 30,000. The food was discontinued and only sips of water allowed by mouth. Three hundred c.c. of physiologic sodium chlorid solution were introduced into the peritoneal cavity at once. Following this, the temperature rose to 101 F. The pulse became stronger and the color better. The vomiting ceased and the patient was given water freely by mouth. The diarrhea continued and on the second day after admission the second intraperitoneal

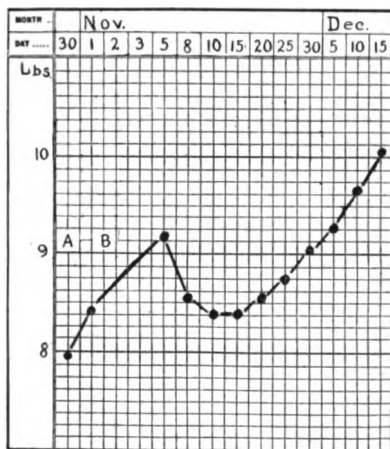


Chart 1.—(M. H., Case 1). Two intraperitoneal injections of physiologic sodium chlorid solution were given; at A, 300 c.c. and at B, 200 c.c. Note the weight curve.

injection of 200 c.c. of physiologic sodium chlorid solution was given. The child remained in a critical condition for several days, after which she began to improve and gained 2 pounds in six weeks.

CASE 2.—E. P., aged 5 months; weight, 10 pounds.

The patient, who had never been breast fed, was brought to the outpatient department because of vomiting and diarrhea. She did fairly well for seven days. Then there was a recurrence with a loss of 14 ounces in two days, and she was admitted to the ward. She presented the usual picture of an infant who had suffered from a severe and prolonged gastro-intestinal disturbance. There were the evidences of prostration—subnormal temperature, pallor and cold extremities—and of great loss of fluids (sunken eyes, pinched expression, dry and inelastic skin and anuria). She was drowsy, except when disturbed, and then she was restless and excitable. There was no hyperpnea. The heart's action was slow and weak. The abdomen was sunken. The temperature was 97 F. The leukocytes were 19,900.

Two hundred c.c. physiologic sodium chlorid solution were introduced into the peritoneal cavity at once. Fluid by mouth was withheld for twelve hours.

Then, as there had been no vomiting, protein milk was given at four-hour intervals and water every hour. There was a febrile reaction lasting twenty-four hours following the intraperitoneal injection. The response to the measures instituted was promptly shown by the improvement in the general condition of the patient. There was no further vomiting and the stools became normal after three days. The protein milk mixture was gradually replaced by a

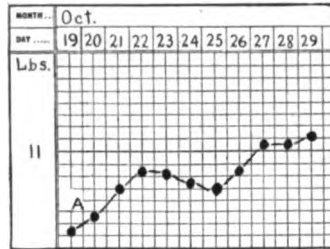


Chart 2.—(E. R., Case 2). Weight curve under treatment with one intra-peritoneal injection of physiologic sodium chlorid solution at A.

whole milk mixture and the patient was discharged, having gained 14 ounces in ten days. Two weeks later, the infant was operated on for an acute mastoiditis, from which she made an uneventful recovery.

CASE 3.—H. E., aged 7 weeks; weight, 6 pounds.

The patient was breast fed for two weeks, then received a cow's milk formula, and as she did not thrive, condensed milk was tried. During this time

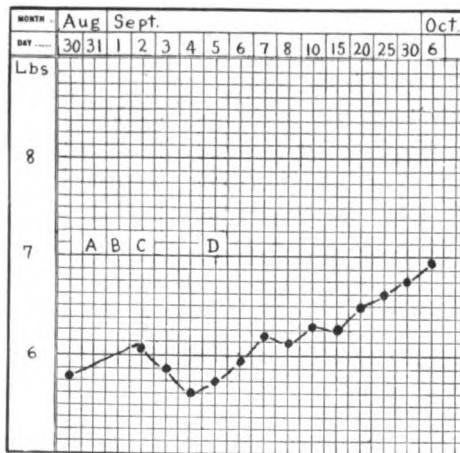


Chart 3.—(H. E., Case 3). Weight curve under intraperitoneal injections of physiologic sodium chlorid solution, 200 c.c. each at A, B, C and D.

vomiting occurred frequently and there was diarrhea. Four days before admission the vomiting and diarrhea became severe and she became rapidly worse.

When admitted to the wards the patient was cyanotic and the hands and the feet were cold. She was extremely restless and had a shrill, piercing cry. There was no hyperpnea. The temperature was 100 F. The leukocytes were 19,000.

The vomiting and diarrhea continued and her condition remained critical for four days. During this time the patient received three intraperitoneal injections of physiologic sodium chlorid solution (200 c.c., 200 c.c. and 150 c.c., respectively). After the third injection the condition of the patient was somewhat improved, she was less restless and the vomiting and diarrhea had subsided. On the seventh day the vomiting recurred and the stools again became loose and watery. The fourth intraperitoneal injection of 150 c.c. of physiologic sodium chlorid solution was given. There was no vomiting thereafter, the stools gradually became normal and she was discharged from the hospital having gained a pound in five weeks.

CASE 4.—G. H., aged 4 months; weight, 7 pounds 2½ ounces.

The patient did poorly after he was weaned at the third month. Condensed milk was given and he was admitted to the hospital because of vomiting which had persisted for two weeks.

He was an emaciated infant with a small amount of subcutaneous tissue. The eyes were sunken, the cry feeble and there were many petechiae on the abdomen. The heart's action was slow and weak; there was no hyperpnea. The temperature was 100 F. Leukocytes were 22,500.

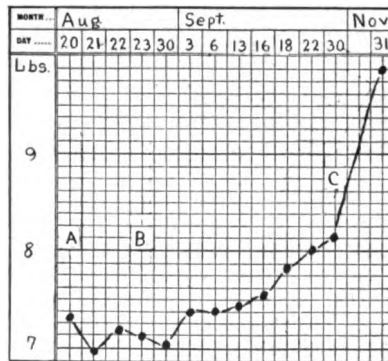


Chart 4.—(G. H., Case 4). Weight curve under intraperitoneal injections of physiologic sodium chlorid solution, 175 c.c. at A and 150 c.c. at B. C, weight two months later.

One hundred and seventy-five c.c. of physiologic sodium chlorid solution were introduced into the peritoneal cavity soon after admission and nothing was given by mouth because of vomiting. The infant's condition became much improved after the injection. There was no vomiting after the first twenty-four hours and he was given buttermilk. Two days after admission a second injection of physiologic sodium chlorid solution, 150 c.c., was given because of a collapse. After this the general condition remained good, although he did not gain. The buttermilk feedings were gradually replaced by breast milk. There was no vomiting and the stools became normal.

The patient was discharged six weeks after admission, having gained 12 ounces. He continued to improve and gained 1 pound and 14 ounces in the following month.

CASE 5.—G. S., aged 4 months; weight, 7 pounds.

The patient was breast fed for two months and then weaned. He did not gain in weight on a condensed milk mixture and when 2 months of age contracted pertussis. He vomited repeatedly after coughing, lost in weight, and for two weeks before admission had from six to eight loose, green, watery stools a day.

He was a very poorly nourished infant. The cry was feeble, there was a grayish pallor of the skin and the abdominal muscles were greatly relaxed. The

heart action was slow. The temperature was 97.5 F. The leukocytes were 18,500.

On admission to the hospital, 200 c.c. of physiologic sodium chlorid solution were injected into the peritoneal cavity. A most remarkable improvement was noted twelve hours later. His color was better, the cry stronger and the heart action more rapid. The stools became normal after three days and he was

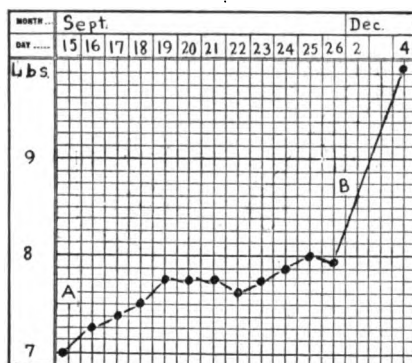


Chart 5.—(G. S., Case 5). Weight curve following treatment by intra-peritoneal injection of physiologic sodium chlorid solution, 200 c.c. at A. B, weight two months after discharge.

discharged in eleven days, having gained 14 ounces. The improvement continued and he gained 2 pounds in two months.

CASE 6.—L. G., aged 5 months; weight, 11 pounds.

The patient was breast fed for two months, then received a cow's milk mixture. He progressed fairly satisfactorily, with the exception of an occasional mild attack of diarrhea. The day before admission he had several large watery stools and became very restless and irritable.

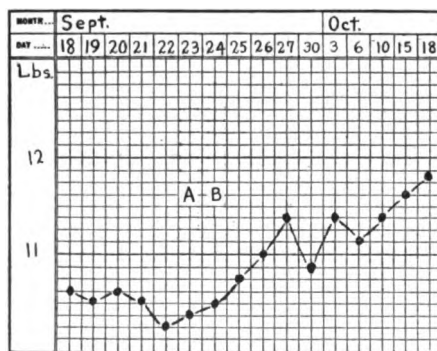


Chart 6.—(L. G., Case 6). Weight curve; 150 c.c. physiologic sodium chlorid solution given at A and B.

The infant was not thought to be particularly ill when admitted to the ward. There was no vomiting and the stools while loose were not very frequent (three to five per day). He was very irritable and restless. There was no hyperpnea. He was treated in the usual manner for five days. There was a loss of 6 ounces in weight and the stools did not improve. On the fifth day he suddenly became worse. There was cyanosis, irregular shallow breathing

and the heart action was rapid. Because of this collapse he was given 150 c.c. physiologic sodium chlorid solution into the peritoneal cavity. This was followed by general improvement in his condition. On the following day a second intraperitoneal injection (150 c.c.) was given. The improvement after the second injection was prompt; his general condition continued to become better and he was discharged at the end of one month, having gained 11 ounces in weight.

CASE 7.—R. D., aged 2 months; weight, 7 pounds.

Because of failure to gain in weight the patient was weaned at 1 month of age and then received feedings of condensed milk. She did well for a time, but two days before admission developed diarrhea and vomiting.

On admission the child showed a moderate degree of malnutrition. The temperature was 101 F. The leukocytes were 12,300. An injection of 120 c.c. of physiologic sodium chlorid solution into the peritoneal cavity caused a marked improvement in the general condition, and alternate feedings of breast milk and buttermilk were begun. The temperature remained elevated and small amounts of the feedings were refused or regurgitated. The stools were loose.

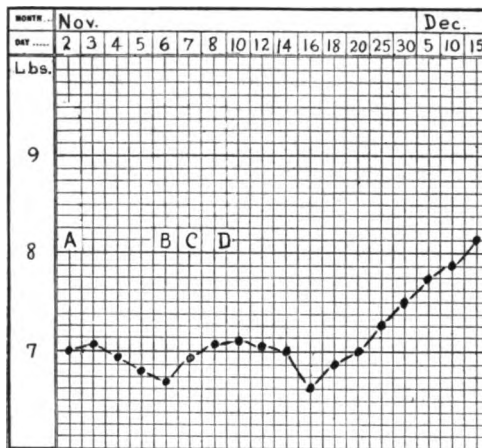


Chart 7.—(R. D., Case 7). Weight curve; intraperitoneal injections of physiologic sodium chlorid solution, 125 c.c. at A, 150 c.c. at B, 100 c.c. at C and 175 c.c. at D.

The fourth day after admission, the infant became much worse and hyperpnea was observed. This suggested an acidosis, which was verified by the laboratory tests. The carbon dioxide tension of the alveolar air was 24 mm. The RpH^a of the blood serum was 7.8. Seventy c.c. of a 4 per cent. solution of sodium bicarbonate were injected into the longitudinal sinus at once; sodium bicarbonate was also given by mouth. One hundred and fifty c.c. of physiologic sodium chlorid solution were injected intraperitoneally and after sixteen hours 100 c.c. were given again. A third injection of 175 c.c. of the saline solution was given in the following twenty-four hours. After the administration of a total of 15 gm. of sodium bicarbonate in twenty-two hours, the carbon dioxide tension in the alveolar air was 38 mm. and the RpH of the blood serum was 8.3.

There was a marked improvement in the patient's condition after the administration of water and of alkali, but she remained in a critical condition for

6. Marriott: Arch. Int. Med., 1916, 17, Part 1, p. 840.

about eight days. After this she began to improve and was discharged after six weeks, having gained 1 pound 2 ounces.

CASE 8.—J. E. W., aged 2½ months; weight, 4 pounds 14 ounces.

The patient did not thrive on woman's milk and was weaned at 1 month of age. He developed diarrhea on cow's milk and was brought to the hospital with convulsive twitchings, cyanosis, short gasping respirations, a subnormal temperature and weak pulse. The leukocytes were 26,800. He had eight loose stools during the first twenty-four hours in the hospital. He was given three intraperitoneal injections of salt solution (of 100, 100 and 160 c.c., respectively) on successive days. He remained in a critical condition for three days. There-

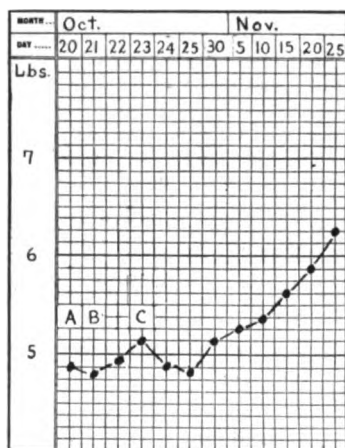


Chart 8.—(J. E. W., Case 8). Weight curve; intraperitoneal injections of physiologic sodium chlorid solution, 100 c.c. at A and B and 160 c.c. at C.

after he began to improve and was discharged from the hospital having gained 1½ pounds in five weeks.

CASE 9.—H. S. (15101), aged 6 months; weight, 11½ pounds.

The baby was breast fed for five months and then received a condensed milk formula. She lost in weight, vomited and had diarrhea on this food, and was brought to the hospital because the vomiting and diarrhea became worse. The patient was admitted to the wards in a critical condition. She was very poorly nourished and very restless. Hyperpnea was present. The laboratory tests showed that there was an acidosis. Blood serum; Ph 7.3; Rph 7.7. The temperature was 104 F. There was constant vomiting and there were seven large and watery stools in twenty-four hours. Treatment was begun at once. All food by mouth was discontinued; 200 c.c. physiologic sodium chlorid solution were injected intraperitoneally, and 75 c.c. of a 4 per cent. solution of sodium bicarbonate were injected intravenously. The child's general condition improved promptly and the respirations became normal in character. A second intraperitoneal injection of the saline solution was given on the following day and sodium bicarbonate was also administered by mouth. The vomiting ceased and on protein milk the stools improved. The temperature gradually became normal and the patient was discharged ten days after admission.

PROGRESS IN PEDIATRICS

REVIEW OF THE COMMUNICABLE DISEASES *

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CHICAGO

THE COMMUNICABLE DISEASES

Epidemiology.—Kelley,¹ believing that the milk supply is often implicated as the channel of infection in epidemics of communicable diseases, when, as a matter of fact, it is the exception to find that any attempt has been made to determine the probable source of infection, tabulated the investigations of the Massachusetts State Board of Health field force, covering outbreaks and epidemics over a period of five years. His analysis does not corroborate the statements recently made in the literature, the experience in Massachusetts indicating that even in raw milk the transmission of diphtheria is so rare as to be negligible, and that the transmission of scarlet fever, though commoner, is of very small percentage significance.

Control.—Josephine Baker² tells us that in New York City the chief reliance for the prevention of the spread of the communicable diseases is placed on the system of school medical inspection. Children are excluded on suspicion; pupils in rooms where contagious diseases have occurred are inspected daily; cultures are taken from all suspected cases; the school doctor inspects daily all children suspected of being ill and all who have returned to school after an illness or unexplained absence. All absentees of more than three days' duration are visited at home. The wisdom of keeping children in school in the presence of communicable diseases is emphasized. Systematic observation offers a greater degree of protection to other children than can be attained by allowing them to mix indiscriminately on the street when the schools are closed. The same writer³ makes further suggestions for the control of these diseases: (1) a broad campaign of public health education, as without the cooperation of the public not much can be accomplished; (2) the keeping of a home record concerning school progress, the occurrence of communicable diseases and the physical welfare of

* Submitted for publication Oct. 15, 1917.

1. Kelley: Jour. Am. Med. Assn., 1916, **67**, 1997.

2. Baker: Am. J. Pub. Health, 1916, **6**, 1078.

3. Baker: New York Med. Jour., 1917, **105**, 1198.

the child; (3) the general use of the Schick test and the immunization of all susceptible children by means of toxin-antitoxin injections; (4) the exclusion from school of all children with a bronchial cold, together with the establishment of whooping cough clinics; (5) more detailed attention to personal hygiene and to the hygiene of the nose and throat.

Hospitalization.—Wilson⁴ says that public sentiment generally is opposed to admitting most cases of a communicable nature to special hospitals, but he advocates giving health authorities the power to order to the hospital cases of communicable disease in every instance in which there is failure to comply with the health laws, and every community should have hospital accommodations sufficient to care for all nonquarantinable cases of this nature. With this control, Wilson is confident that there would never be an epidemic in the accepted definition of the term.

Caverly⁵ calls attention to the fact that house quarantine is at best cumbersome, unscientific and often ineffective, and favors the establishment of isolation hospitals or wards connected with general hospitals, especially in rural communities, the latter combining, by towns or counties, in their support.

Quarantine and Disinfection.—Hubbard⁶ sent a questionnaire to sixteen of the largest municipalities regarding the procedure in the case of the communicable diseases. He found that some cities are ultraconservative, and concludes that while no one knows the best, safest and most economical method of prevention and control of these diseases, it should be appreciated that the most desirable system will be that which is freest from unnecessary restraint and at the same time is consistent with demonstrated methods and scientific knowledge. Williams⁷ questioned eighteen prominent physicians regarding the minor communicable diseases, and decides that all three should be reported if any attempt is to be made to control and abolish them; chickenpox, because it is sometimes confused with smallpox, and because it may be a serious disease itself; German measles, because of its frequent confusion with scarlet fever; and mumps, because it may be more serious than commonly supposed.

Laubach⁸ found that pathogenic bacteria can seldom be isolated from books handled by the sick and, consequently, there is no reason for believing that they may serve as vehicles of infection, although the

4. Wilson: Am. Jour. Pub. Health, 1916, **6**, 261.

5. Caverly: Am. Jour. Pub. Health, 1916, **6**, 1196.

6. Hubbard: Jour Am. Med. Assn., 1915, **65**, 1781.

7. Williams: Albany Med. Ann., 1916, **37**, 343.

8. Laubach: Bull. Johns Hopkins Hosp., 1916, **27**, 183.

fact that pathogenic bacteria can be recovered from artificially infected books after a long period of time, is sufficient reason for disinfection of the latter. Knause⁹ holds that mediary disinfection is a most important factor in the control of communicable diseases, and thinks it is neglected by both the attending physician and the health authorities. Terminal disinfection by cleaning and renovation is desirable from a sanitary and a psychological point of view, but fumigation is costly, and as a factor in the control of these diseases it is of negative value. Walcott¹⁰ thinks that a safe working rule is to scrub with soap and water as high as a man can reach the room in which a patient has been ill. When fumigation is discontinued, a good many dollars will be released to be spent to better advantage.

Aseptic Nursing.—Richardson¹¹ of Providence reports on the occurrence of cross infections among 4,689 patients suffering from communicable diseases, cared for during the period March 1, 1910, to Jan. 1, 1916, using aseptic nursing technic. The percentage of cross infections was 3.5. Richardson concludes that it is fair to state that air infection is a rare occurrence and that rigid asepsis is of primary importance. Hospitals for communicable diseases should not have wards of over six to ten beds each, and should be provided with a sufficient number of smaller units to accommodate all new patients for an observation period.

Cowie¹² recites his experience with 223 cases in the communicable disease division, using the aseptic technic method as practiced in Providence. Only five instances of cross infection occurred, apparently the result of faulty technic on the part of one nurse. His objections to the method are the danger from incubating cases and from diphtheria carriers among the nurses and attendants. Actual experience, however, has tended to minimize in his mind the probable danger from either of these sources. Miss Burby¹³ reports only one cross infection in two years, in the communicable disease wards of the New London Memorial Hospital, while two nurses contracted diphtheria. Aseptic technic is practiced, each room being equipped with running water and each nurse being required to wash her hands after doing or touching anything in the line of duty, no matter how trivial.

Wilson¹⁴ agrees that communicable diseases can be treated in general hospitals and that other patients can be guarded against infection.

9. Knause: *Am. Jour. Pub. Health*, 1916, **6**, 364.

10. Walcott: *Boston Med. and Surg. Jour.*, 1916, **174**, 337.

11. Richardson: *Am. Jour. Pub. Health*, 1916, **6**, 995.

12. Cowie: *Jour. Mich. Med. Soc.*, 1916, **15**, 240.

13. Burby: *Mod. Hosp.*, 1916, **7**, 306.

14. Wilson: *Mod. Hosp.*, 1916, **7**, 316.

Thomson¹⁵ has kept very careful track of 497 patients suffering from 657 communicable diseases that were treated in a twelve-bed ward over a period of some three and a half years. He concludes that scarlet fever, diphtheria, rubella and mumps are not air borne; that whooping cough may be; and that chickenpox is air borne, early in the disease.

Incubation Period.—On the basis of the work done by Bull,¹⁶ it is suggested¹⁷ that the incubation period of the communicable diseases is due to the fact that the infecting agents must become adapted to the adverse conditions encountered in the newly infected host before they can multiply sufficiently to produce symptoms of disease. It is further suggested that epidemics may arise because the infectious agent is passed from person to person in the ascending stage of the disease, and thus enters new hosts in a state of maximum resistance to the natural antibodies of such individuals. When early contacts are avoided, epidemics tend to subside because the infectious agent is weakened by the action of acquired antibodies during convalescence.

Death Rate.—Studying the death rate from the acute infections, Graham¹⁸ found that among infants less than 1 year old, whooping cough caused more deaths than measles, diphtheria or scarlet fever. Measles showed the next highest mortality, then diphtheria, and lastly, scarlet fever. During the second year, diphtheria caused more deaths than either of the others, while more deaths occurred from measles during the second year than at any other period. From the second to the fifth year diphtheria is the most serious, scarlet fever is next, measles is a close third, and whooping cough is not far behind. From the second to the tenth year the diphtheria mortality is higher than that of all other acute infections combined.

Royer¹⁹ presents statistics to show that public health control has been responsible in part for the decline in the measles death rate from a yearly average of 1,300 to approximately 700; that there has also been some decline in the diphtheria death rate and in that from whooping cough. How much of the latter depends on public health activities is doubtful, while Royer feels that scarlet fever has not shown the same tendencies to yield results from public health control.

Kelley²⁰ believes that the achievements of preventive medicine during the past twenty years have been striking, especially in reducing the mortality rate from diphtheria and certain other infections, but it is

15. Thomson: *Lancet*, London, 1916, **1**, 341.

16. Bull: *Jour. Exper. Med.*, 1916, **24**, 7.

17. Editorial: *Jour. Am. Med. Assn.*, 1916, **67**, 1305.

18. Graham: *Jour. Am. Med. Assn.*, 1916, **67**, 1272.

19. Royer: *Penn. Med. Jour.*, 1916, **19**, 432.

20. Kelley: *Boston Med. and Surg. Jour.*, 1915, **173**, 163.

not so good in scarlet fever, measles and whooping cough. To further reduce the prevalence of the communicable diseases the following means must be looked to: (1) better education of the public as to the real nature of communicable disease transmission; (2) more efficient diagnoses; (3) prompt reporting to the authorities; (4) efficient isolation.

While the death rate as a whole, and for certain diseases, shows a decrease in the past year (1916), that for measles and whooping cough, according to Veeder,²¹ remains practically the same, between 9,000 and 10,000 deaths occurring annually in the United States from those diseases. Somewhere between 5 and 10 per cent. of the mortality of the first year of life which may be lessened, is due to measles and whooping cough.

Treatment.—Goodridge,²² reviewing the subject of circulatory failure in the acute infections, concludes that there is neither clinical nor experimental evidence in support of the belief that failure of the vasomotor center is the cause of the symptoms of circulatory failure which occurs in these diseases. He finds alcohol and strychnin absolutely worthless in the treatment of circulatory failure. Epinephrin and pituitary extract are useful in sudden circulatory collapse, but their action is not a sustained one.

Lemoine and Devin²³ used Milne's²⁴ method of prophylaxis in the treatment of measles, scarlet fever, mumps and diphtheria, without the development of any cross infections or complications. They believe that when the method is painstakingly applied, the period of isolation after the communicable diseases can be materially shortened. Other French clinicians²⁵ report excellent results with the same method, chiefly in scarlet fever.²⁶

GERMAN MEASLES

Few articles have appeared during the past two years on the subject of rubella, and these have been chiefly clinical reports.

Comby,²⁷ from his observations on 132 cases, believes the disease to be an eruptive fever, distinct from measles and scarlet fever. The scarlatiniform variety of rubella is not a distinct affection, as claimed by Duke,²⁸ but only a form of German measles.

21. Veeder: Arch. Pediat., 1917, **34**, 321.

22. Goodridge: Am. Jour. Med. Sc., 1917, **153**, 107.

23. Lemoine and Devin: Bull. de l'Acad. de méd., 1916, **75**, 385.

24. Milne: Lancet, London, 1911, **1**, 1070.

25. Vevey: Bull. gén. de therap., 1915-1916, **168**, 831.

26. Chantemesse: Bull. de l'Acad. de méd., 1915, **74**, 681.

27. Comby: Arch. de méd. d. enf., 1916, **18**, 293.

28. Duke: Lancet, London, 1900, **2**, 89.

Gray²⁹ reports 283 cases, one third of which had had a previous attack. Six cases ended fatally, a mortality of 2.1 per cent. Box³⁰ analyzes 850 cases and finds that previous attacks undoubtedly occurred in twenty-six of these. All observers agree that the incubation period is long, between twelve and twenty days. Lewis³¹ believes that "German measles" is not a diagnosis, and as such is unnecessary in medical nomenclature. He thinks that so-called German measles is either true scarlet fever, measles or true grippé.

Adamson³² reports two cases of the so-called fourth disease of Duke,³³ both with two relapses each.

Greeley³³ has continued his work with the diplococcus-like organism which he found to be constantly present in varicella vesicles, and has been able to cultivate the organism on artificial mediums. He has conducted agglutination and complement fixation tests, but does not find that specific value can be attached to agglutination tests, the varicella antigen giving negative results with the corresponding serums and positive tests with most normal serums tried.

Kolmer³⁴ showed that an antibody in the nature of an amboceptor is present in the serum of persons suffering with varicella, and will absorb complement in the presence of an antigen prepared from the cutaneous lesions of the disease. The percentage of positive reactions, and particularly the degree of complement fixation, is small, however.

Experimenting with protective chickenpox vaccination after the manner of Kling,³⁵ Sophie Rabinoff³⁶ found the chief difficulty in obtaining the virus. Animal experimentation thus far has been unsuccessful, and it is necessary to use material directly from either the vesicles or pustules from an active case of the disease. Among 142 susceptible children, 114, or about 75 per cent., developed varicella, while in a group of 76 vaccinated children, only 6, or about 8 per cent., contracted the disease, all of them, however, within the incubation period, which was about sixteen days. The duration of the protection could not be determined.

Thomson¹⁵ is convinced that chickenpox is air borne early in the disease, it rarely being carried in the air as late as the third day, but apparently not afterward. Thomson exposed susceptibles suffering from scarlet fever to cases of scarlet fever and chickenpox. The last

29. Gray: *New York Med. Jour.*, 1915, **94**, 104.

30. Box: *Practitioner*, 1917, **98**, 501.

31. Lewis: *Boston Med. and Surg. Jour.*, 1917, **176**, 742.

32. Adamson: *Lancet*, London, 1916, **1**, 290.

33. Greeley: *Med. Rec.*, New York, 1916, **90**, 265.

34. Kolmer: *Jour. Immunol.*, 1916, **1**, 59.

35. Kling: *Berl. klin. Wchnschr.*, 1913, **50**, 2083.

36. Rabinoff: *Am. Jour. Obst.*, 1915, **72**, 526.

case was introduced as early as the eighth day of the chickenpox, and yet no infection resulted, but it has not been determined just how early the chickenpox patient ceases to be a danger to those with whom he comes in contact. Enough has been accomplished to show that it is needless to keep varicella patients separate from others as long as it has been generally supposed necessary.

Several clinical cases are reported. Wyler³⁷ tells of a corneal ulcer complicating chickenpox, which he believes to be the eruption of a pock. Smith³⁸ observed a case which showed symptoms indicating unmistakably the existence of a lesion in the cord, an acute myelitis. Campbell³⁹ reports a hemorrhagic chickenpox in an infant 5½ months old, with death twenty-seven hours after the onset of the hemorrhages. Guidi⁴⁰ saw a case of varicella with localization in the larynx, necessitating intubation.

MUMPS

From experiments conducted on cats, Wollstein⁴¹ deduces that the salivary secretion in mumps contains a filterable substance capable of setting up a series of definite pathologic changes when inoculated into the testicle and parotid glands of that animal. Whether this active material contains a micro-organism, and if it does, whether it is the specific microbic cause of mumps, remains to be seen.

Feiling⁴² presents a critical review of the entire subject of mumps, with a table of forty-one examinations of the blood. Twenty-one of these patients had a white count somewhere between 6,000 and 10,000, the highest 15,600; the rest were below 6,000, the lowest being 4,600. In every case there was a lymphocytosis, either relative or absolute.

Marcovici⁴³ examined the blood of ten cases of uncomplicated mumps, first on the second or third day, and again on the tenth. In the early stages the count was normal, ranging from 5,900 to 7,150, the mononuclears being increased at the expense of the neutrophils, and the eosinophils being normal or entirely absent. In the second stage there is a leukocytosis of the neutrophilic type, ranging from 10,000 to 20,000, with an increase of the eosinophils to 7 per cent.

The most interesting work on mumps, however, is that of Hess,⁴⁴ who attempted to confer immunity to the disease by the use of blood from convalescent patients. He inoculated twenty children who had

37. Wyler: *Jour. Am. Med. Assn.*, 1917, **68**, 1476.

38. Smith: *AM. JOUR. DIS. CHILD.*, 1915, **10**, 445.

39. Campbell: *Canada Med. Assn. Jour.*, 1915, **5**, 610.

40. Guidi: *Riv. di clin. pediat.*, 1915, **13**, 435.

41. Wollstein: *Jour. Exper. Med.*, 1916, **23**, 353.

42. Feiling: *Quart. Jour. Med.*, 1915, **8**, 255.

43. Marcovici: *Folia hematol.*, 1915, **20**, 136.

44. Hess: *Am. Jour. Obst.*, 1915, **72**, 183.

never had mumps with the blood of convalescents, using 6 or 8 c.c. from the vein in the elbow and injecting it intramuscularly. Four of these children were inoculated from patients who had just recovered and in whom there was still some parotid swelling. A second group were inoculated from patients about ten days recovered, while the third group received blood from children who had had the disease several years previously. All the children were put into mump wards, but not one of the inoculated children contracted the disease, while in one ward eleven susceptible children contracted the infection. The blood from old cases seemed to be just as efficacious as that from recently recovered patients.

Case Reports.—Lavergne⁴⁵ saw symptoms of meningitis precede those of mumps, and this suggested the possibility that certain conditions described as "meningeal states" may have been parotid meningitis, with which the inflammation of the parotid glands was too slight to attract attention. Josephson⁴⁶ encountered a suppurative process in the right adnexa secondary to an attack of mumps, and believes that this demonstrates that the latter disease is a general infection which is liable to attack any of the glands. As a rule, the testicles bear the brunt of the attack, secondary to the parotids, the ovaries and the mammary glands coming next in frequency. Chillingworth⁴⁷ reports a case which apparently affected the pancreas first, then the left ovary, then the right ovary and finally both parotids simultaneously.

Voisin⁴⁸ saw a fatal case of meningitis complicating mumps; Batigne⁴⁹ reports a case of orchitis as a complication; Sainton and Bosquet⁵⁰ tell of a case of typical mumps complicated by cerebrospinal meningitis, the latter verified bacteriologically; Sainton and Huriez⁵¹ observed a rare complication of mumps, a double paralysis of the brachial plexus; Massary and Tockmann⁵² analyzed a series of 243 cases of mumps, of which fifty-nine, or 24 per cent., developed orchitis, and fifty-six, or 23 per cent., developed a meningeal reaction; Eichhorst⁵³ reports two cases of mumps in which bradycardia was especially striking. He believes the condition to be due to a toxin.

45. Lavergne: Arch. de méd. d. enf., 1917, **20**, 182.

46. Josephson: Upsala Läkaref. Förh., 1915-1916, **21**, 523.

47. Chillingworth: Brit. Med. Jour., 1916, **1**, 653.

48. Voisin: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 223.

49. Batigne: Ann. d. mal. ven., 1916, **11**, 340.

50. Sainton and Bosquet: Bull. de l'Acad. de méd., Paris, 1915, **74**, 368.

51. Sainton and Huriez: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 809.

52. Massary and Tockmann: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 1035.

53. Eichhorst: Med. Klin., 1915, **11**, 535.

Bertelsen⁵⁴ relates his experience with mumps which was brought to Greenland in 1913. Of the 2,425 individuals in the district, about 1,500 contracted the disease. No infant under 2 years of age was affected.

WHOOPING COUGH

Epidemiology and Prophylaxis.—The best hope for good results in the control of whooping cough, according to Crum,⁵⁵ lies along educational lines, physicians, teachers, nurses, parents and older children all needing information as to how the presence of the disease may be detected and what to do when it is discovered. Intensive statistical study of the disease is necessary, and if properly conducted would go far to remove the present widespread ignorance of the disease, the gravity of which is not appreciated either by the general physician or the public.

In Morse's⁵⁶ opinion the greatest obstacles to the control of the disease are the facts that the early symptoms are so indefinite that it is most contagious at the time when it is impossible to recognize it clinically, and that extremely mild types are common. It is evident that while examination of the blood and sputum and the complement fixation test are of undoubted value in the diagnosis of whooping cough, they are not at present of great practical utility in the recognition and prevention of the spread of the disease. Isolation of the sick, especially from babies and young children, should be insisted on, and if this is impossible, the cases should be sent to hospitals constructed on the "shack" plan, in order to give the children the maximum amount of fresh air. Morse does not believe that isolation should be maintained beyond the fifth or sixth week.

Abt⁵⁷ urges that all concerned in the prevention of disease cooperate to enforce such regulations as will prevent those sick with whooping cough from attending school, visiting playgrounds and using public conveyances, and in isolating those sick or suspected of being sick with the disease.

Tissier⁵⁸ reports that in a recent epidemic the adult more often transmitted the disease to the child than vice versa, which is contrary to what is usually the case.

Pathology.—Rhea⁵⁹ describes the lesions present in the trachea and bronchi of dogs ill with distemper, and calls attention to the similarity

54. Bertelsen: Ugesk. f. Laeger., 1915, **77**, 1925.

55. Crum: Am. Jour. Pub. Health, 1915, **5**, 994.

56. Morse: Boston Med. and Surg. Jour., 1916, **175**, 723.

57. Abt: Jour. Am. Med. Assn., 1916, **67**, 1787.

58. Tissier: Bull. de l'Acad. de méd., Paris, 1916, **75**, 690.

59. Rhea: Jour. Med. Research, 1915, **32**, 471.

of these lesions to those in human beings who have succumbed to whooping cough. He warns that the interpretation of the results following experimental inoculation of the respiratory system of dogs, guinea-pigs and rabbits with *B. pertussis* cannot safely be based on histologic examination alone. *B. pertussis* must be recovered from the respiratory system of the inoculated animal and completely identified by bacteriologic methods as well as by agglutination reactions. Rhea suggests further that when the respiratory system of an animal liable to harbor *B. bronchisepticus* is experimentally inoculated with *B. pertussis*, the accompanying irritation might be followed by symptoms resulting from *B. bronchisepticus* already present and not from *B. pertussis* injected.

Complement Fixation.—Olmsted and Luttinger,⁶⁰ working with complement fixation in whooping cough, found that the most reliable antigen is obtained by autolyzing an aqueous emulsion of a twenty-four to forty-eight-hour growth of the Bordet-Gengou bacillus for eighteen to twenty-four hours at 56 C., and then shaking for several hours. An active serum, they found, sometimes gave nonspecific reactions; therefore a negative reaction given by an active serum is stronger evidence of lack of infection than is a negative reaction given by an inactive serum. About 40 per cent. of whooping-cough cases gave positive reactions when inactive serum was used, the highest percentage of positives being given by convalescent, vaccinated patients. They conclude that their results support the theory that the Bordet-Gengou bacillus is the etiologic factor in the disease, and think that the complement fixation test may be of value in the diagnosis of doubtful cases of pertussis.

Somewhat later, Povitsky and Worth⁶¹ obtained a strongly agglutinating pertussis serum from the rabbit by ten or twelve intraperitoneal inoculations of living cultures given at seven-day intervals. Vaccines also produced agglutinins, but not as markedly as the living cultures. By agglutination tests *B. pertussis* strains can be specifically identified, according to these workers, from hemoglobinophilic bacilli, pertussis-like bacilli and *B. bronchisepticus*.

For purposes of identification, a strong serum of high titer should be used. Thirty-three per cent. of adult nonpertussis serums show agglutination in up to 1:40; 17 per cent. in up to 1:100; 40 per cent. of children's nonpertussis serums showed a reaction up to 1:40. A dilution of not less than 1:200 is necessary for a practically positive diagnosis of pertussis by the agglutination test.

60. Olmsted and Luttinger: Arch. Int. Med., 1915, 16, 67.

61. Povitsky and Worth: Arch. Int. Med., 1916, 17, 179.

Olmsted and Povitsky⁶² confirmed the separation, by morphologic and cultural characteristics, of typical Bordet-Gengou bacilli from atypical strains and from the influenza bacillus by the complement fixation tests. Twelve strains of *B. pertussis* isolated by them from patients with pertussis gave complement fixation reactions similar to each other and similar to the two strains obtained from other laboratories.

Jacobsen and Mayer⁶³ conclude from their work with complement fixation, using the Bordet-Gengou bacillus as antigen, that a positive reaction means the individual has or has had whooping cough recently, while a negative reaction does not prove absence of the disease. On the basis of this they believe the Bordet-Gengou bacillus should be regarded as the specific cause of the disease.

Blood.—Mello-Leitao⁶⁴ studied the refractometric index of the blood in whooping cough as well as in measles, and believes that it permits differentiation of the former from tuberculous tracheobronchial adenopathy.

Benstz⁶⁵ tabulates the blood findings in sixty-three cases of whooping cough in infants under 1 year and children up to 6 years. There was always leukocytosis, most pronounced when bronchitic complications were present. The number of eosinophils was always below normal, while transitional and mononuclear forms were much increased, reaching 18 per cent. at the height of the disease.

Symptoms, Sequelae and Diagnosis.—Depping⁶⁶ reports two cases of intussusception as a sequel of whooping cough, both resulting fatally.

Kornmann⁶⁷ saw hematuria occur in otherwise normal urine with healthy kidneys, on an average of five days before the onset of the spasmodic cough. He believes that a toxin must have damaged the kidneys and their blood vessels.

Jacob⁶⁸ calls attention to a marked conjunctival congestion in the region of the external canthus as very suggestive of whooping cough in the earliest stages of the disease.

Morbidity and Mortality.—Eighty per cent. of all cases, according to Luttinger,⁶⁹ and 97 per cent. of all deaths are in children under 5 years of age. Fifty per cent. of patients are under 2 years of age and

62. Olmsted and Povitsky: Jour. Med. Research, 1916, **33**, 379.

63. Jacobsen and Mayer: Arch. f. Kinderh., 1915, **14**, 32.

64. Mello-Leitao: Am. Jour. Dis. Child., 1916, **11**, 214.

65. Benstz: Nederl. Tijdschr. v. Geneesk., 1916, **1**, 153.

66. Depping: U. S. Naval Med. Bull., 1916, **10**, 319.

67. Kornmann: München. med. Wchnschr., 1915, **62**, 1422.

68. Jacob: Brit. Med. Jour., 1916, **1**, 589.

69. Luttinger: Am. Jour. Dis. Child., 1916, **12**, 290.

50 per cent. of deaths are in children under 1 year. The incidence of pertussis and the number of deaths are constantly higher in girls, 44 and 56 per cent., respectively, in the male and female sexes. Whooping cough is most common in the spring and summer, the mortality curve reaching its height in August. The actual mortality is hard to estimate, but it is probably about 1 per cent., and the death rate per 100,000 of population is about 7.

The mortality of whooping cough in the year 1915 in the registration area⁷⁰ was 8.1 per 100,000, somewhat above the lowest recorded rate, 6.5 in 1904, although far below the highest, 15.8 in 1903.

Crum⁷¹ made a statistical study of the disease and shows that 1 per cent. of the grand total of deaths from all causes in twenty-four countries was due to whooping cough. Climate is probably of secondary importance either in the spread of the disease or in the determination of its type. Differences of race or nationality do not create either a predisposition or an immunity. The mortality is decidedly higher among female children of all ages, but not more than 2 or 3 per cent. of the total mortality occurred at the age of 5 years or over. The death rate in the first year of life is two and one-half times as great as in the second year, the disease being more fatal at young ages than measles.

Vaccine Treatment.—The prophylactic and curative effects of whooping cough vaccines have received considerable attention during the past two years. In 1916 Luttinger⁷² declared that vaccines, when given early, have continued to give good results, both prophylactic and curative. In 1917 he⁷² reiterates his belief in their efficacy and states that the effects obtained warrant the routine administration of pertussis vaccine for both purposes. He finds that the best time to institute curative vaccine treatment is in the first and second weeks of the paroxysmal stage. When the proper vaccine is given and the proper method of administration is employed, the disease is materially reduced in duration and severity.

Nine patients who had been given prophylactic injections did not contract pertussis, but developed subconjunctival hemorrhages. This fact, Luttinger thinks, points to the specific immunizing action of the vaccine against the paroxysms and to the likelihood that the Bordet-Gengou bacillus elaborates a toxin which acts on the walls of certain blood vessels.

The plan of treatment followed in the whooping cough clinics in

70. Jour. Am. Med. Assn., 1916, **67**, 1457.

71. Crum: Am. Jour. Pub. Health, 1915, **5**, 994.

72. Luttinger: Jour. Am. Med. Assn., 1917, **68**, 1461.

New York City,⁷³ consists in giving three or four subcutaneous injections, one every other day, and following this with an antipyretic mixture for three or four days. The initial dose for children under 1 year is 250 million, doubled every second day. Children over 1 year receive an initial dose of 500 million and adults 1 billion. Under this treatment the paroxysmal stage has been limited on an average to a duration of about three weeks. Prophylactic immunization has been practiced in forty-five cases with no disease among the patients treated. A fair percentage of controls became infected.

Bloom⁷⁴ gives a large initial dose, not less than 120 millions, increasing 60 million each succeeding dose, giving the maximum quantity every other day until one of the marked symptoms showed an appreciable improvement, then continuing every three or four days until cured. He found the average duration of fifteen cases to be only twenty-eight days, and that the intensity and number of the coughing spells and the vomiting lessened or ceased.

Shimer⁷⁵ found that the vaccine controlled the cough and vomiting, but that the beneficial effects rarely lasted for more than thirty-six to forty-eight hours. Its use, however, seems to shorten the length of the disease by two or more weeks. Frankel⁷⁶ injected ten babies with pertussis vaccine and none of them contracted the disease, although in constant contact with it.

The most pessimistic utterances regarding the value of the vaccines emanate from Von Sholly, Blum and Smith.⁷⁷ Their study of a series of whooping-cough cases shows that since whooping cough vaccine statistics under present conditions must be based chiefly on reports of the parents, one must be careful in accepting what they say. Their figures show that nonspecific influenza vaccine differs very little from pertussis vaccine in influencing the duration of the paroxysmal stage of the disease. Of all the cases, the shortest course was run in the nonvaccinated controls and in those receiving milk-colored water. None of the patients inoculated with either pertussis or influenza vaccines contracted the disease. Of 700 children exposed in their families, 24.8 per cent. escaped the disease, and in view of this rather large number of natural immunes, and the fact that influenza vaccines apparently act the same, they ask, can one be sure that pertussis vaccines actually confer immunity? These observers conclude that more observations and more critical observations with controls for comparison must be undertaken

73. Monthly Bull., New York Health Dept., November, 1915.

74. Bloom: New Orleans Med. and Surg. Jour., 1916, **69**, 200.

75. Shimer: Lancet-Clinic, 1916, **116**, 7.

76. Frankel: Kentucky Med. Jour., 1915, **13**, 458.

77. Von Sholly, Blum and Smith: Jour. Am. Med. Assn., 1917, **68**, 1451.

before the case can be considered made out for the curative and prophylactic value of a specific pertussis vaccine.

Other Methods of Treatment.—Hoag⁷⁸ found that in his hands sodium bromid and antipyrin gave the best results of any drugs, but he thought that vaccines seemed effective in any stage. As a prophylactic his experience has been absolutely favorable.

Polozker⁷⁹ reports on 100 cases in which various forms of treatment were tried, with little success in favorably affecting the course. His experience with the vaccine has been encouraging and he declares that he will continue its use.

Ebstein⁸⁰ has found that diathermia of the larynx, applied from each side, has a remarkable attenuating effect on whooping cough, transforming it into an ordinary cough, with which the night rest is no longer disturbed. Ordinary electricity is not enough; it must be the electric waves of the diathermia technic applied for five to ten minutes once or twice to each side of the neck with a current of 0.25 to 0.6 ampere. It causes no sensation except that of warmth, so that children do not object to it.

Doernberger⁸¹ believes that the best means of relief from whooping cough is pure air, free from soot or dust. This is hard to obtain, and he suggests that a part of the public parks be fenced off for whooping cough children.

Benstz⁸² tried many drugs, but no favorable effect was noted from most, though some beneficial action was seen after the use of extract of belladonna, from 1 to 6 mg. three times a day.

Peutz⁸³ injected serum from a convalescent whooping cough child into three others who seemed to be just developing the disease. A mitigating influence seemed unmistakable, but he regrets the smallness of the series.

Kraus⁸³ caught sputum of the first stage of whooping cough in sterile Petri dishes, washed it, examined it for tubercle bacilli, then mixed it with ether and shook it mechanically for several days. The ether was then evaporated and the fluid tested for sterility. The sterile fluid was injected subcutaneously in quantities of 1 or 2 c.c. every three or four days. Almost without exception there was improvement. The number of attacks decreased, the spasmodic cough became more catarrhal in character, the vomiting soon ceased, and hemorrhages, if present, disappeared. Kraus received an impression of great improvement from the treatment.

78. Hoag: *Am. Med.*, 1916, **11**, 255.

79. Polozker: *Am. Jour. Obst.*, 1916, **73**, 551.

80. Ebstein: *München. med. Wchnschr.*, 1916, **63**, 45.

81. Doernberger: *München. med. Wchnschr.*, 1917, **63**, 1691.

82. Peutz: *Nederl. Tijdschr. v. Geneesk.*, 1917, **1**, 714.

83. Kraus: *Wien. klin. Wchnschr.*, 1915, **28**, 1405.

MEASLES

Etiology.—During a period of four years Tunnicliff⁸⁴ has blood cultured fifty patients in the preeruptive and eruptive stages of measles, and five when the rash was fading, using various mediums, both aerobic and anaerobic. A small micrococcus was observed in forty-two of the early cases, the largest number of positive cultures being obtained in semicoagulated horse serum and whole blood ascites dextrose agar shake cultures. Growth appeared in the original tubes in from one to twenty-two days. Twenty-eight of the forty-two positive cultures grew slightly for two or three generations only. One remained strictly anaerobic, while thirteen became aerobic in the second generation. The special points of interest are the almost constant presence of a diplococcus in the blood of measles patients during the preeruptive and eruptive stages; its presence alone and in large numbers before the appearance of the eruption, and alone in a large proportion at the height of the infection, and its presence at the same time in the throat, nose and eyes.

Epidemiology and Prophylaxis.—Wagener,⁸⁵ studying measles epidemics, found nothing to lead him to believe that measles can be transmitted by fomites or carriers. He clearly traced the sequence of events in one-room school houses. The pupils became infected by one or more children who had been exposed outside. Each infects those in the immediate vicinity and these in turn infect others, until by the end of the third week all have become infected. This is followed by infection of children at home of preschool age and of adults.

No child escaped the disease who was exposed for the first time after the age of 5 months. None under 4 months contracted the disease and only one of 5 months. Wagener thinks it is possible that young infants escape because they breathe only through the nose, and thus the measles germs do not have access to the throat. If the infant's nose is stopped up this protection is lost. He calls attention to the fact that 49 per cent. of persons who had already had typical measles developed symptoms on the part of the upper air passages, digestive tract, etc., while other members of the family were having measles. He believes these symptoms were due to the measles germs, and that these persons were, for the time being, carriers.

Lewis⁸⁶ believes that in attempts to control measles the carriers of convalescence must be recognized. They may be identified, according to him, by the presence of an inflammatory condition of the mucous membrane of the nose, tongue and throat.

84. Tunnicliff: Jour. Am. Med. Assn., 1917, **68**, 1028.

85. Wagener: Monatsch. f. Kinderh., 1916, **13**, 477.

86. Lewis: Boston Med. and Surg. Jour., 1917, **176**, 742.

Curtis⁸⁷ is of the opinion that present methods of isolation, placarding, fumigating, etc., have reduced the attack rate appreciably. The question of how to exercise control of this disease, which is considered harmless by the laity, is difficult of solution, and under present conditions, probably not practicable. Public education and the discovery of some certain method of early diagnosis may solve the problem.

Whyte⁸⁸ observes that as most cases of measles are well into the eruptive stage before they are seen by the physician, any measures decided on to cope with the situation should be directed¹ toward the control of the movements of contacts rather than to prolong isolation of the original case. Quarantine and observation of contacts for fourteen days from the date of last exposure would seem to be the only effective measure in preventing the spread from house to house. If it were possible to provide a routine examination for Koplik's spots during the second week of quarantine, many cases could be put under strict isolation during the period when such a measure would be of some value. Gray⁸⁹ believes that for the control of measles it will be necessary to educate parents to the importance of the disease, and to train teachers to recognize the prodromal symptoms. Susceptibles who have been exposed need not be restricted for seven days after contact, but should thereafter be quarantined for at least ten days.

Wilson⁹⁰ would approach the problem of measles prevention along the following lines: (1) standardization of present laws and adoption of the same by all health boards; (2) early detection of cases, to be accomplished by cooperation of the school and health authorities with the family physician; (3) a complete reform of hospital construction so that hospitalization may be made both popular and efficient; (4) a persistent effort to isolate the causative organism in order that an intelligent effort may be made to produce artificial immunity.

Immunity.—Herrman⁹¹ says that infants under 2 months of age are absolutely immune to measles, this immunity gradually lessening until by the eighth month it has entirely disappeared. It is not conveyed through the breast milk, for artificially fed infants are also immune.⁹² The gradual disappearance of immunity is shown by the lengthening of the period of incubation. Apparently only those are immune whose mothers have had the disease, and frequently those infants who are exposed at an early age without contracting the disease are not infected

87. Curtis: *Am. Jour. Pub. Health*, 1916, **6**, 265.

88. Whyte: *Canada Pract. and Rev.*, 1916, **41**, 336.

89. Gray: *Jour. Infect. Dis.*, 1915, **17**, 559.

90. Wilson: *Arch. Pediat.*, 1917, **34**, 241.

91. Herrman: *Am. Jour. Obst.*, 1916, **74**, 551.

92. Herrman: *Arch. Pediat.*, 1917, **34**, 38.

when exposed in later life. Herrman⁹³ attempted to immunize artificially forty infants under 5 months of age by inoculating the nasal mucous membrane with mucus collected from otherwise healthy children, taken twenty-four hours before the measles eruption appeared. The majority showed no distinct reaction, fifteen showed a slight rise of temperature, and in a few instances a small number of spots were noted on the face and body. Of the forty inoculated, four now over a year old have come in contact with cases of measles and have not contracted the disease. Two were reinoculated at the age of 21 and 23 months, respectively, with negative results.

Signs and Symptoms.—Gray⁹⁴ studied an epidemic of 254 cases of measles and found that the minimum period from exposure to the first symptom was seven days, the maximal fourteen days and the average eleven days. The minimal period from the first symptom to the appearance of the exanthem was one day, the maximal seven days and the average three days. The minimal period from exposure to the appearance of the exanthem was eleven days, the maximal nineteen days, the average thirteen and a half days. The incidence of the disease was greatest in males at 6 years of age, and in females at 8 years.

Gardner⁹⁴ thinks that the tongue of measles is characteristic. It is glazed, with a moderately heavy dull-white furring down the center. On the posterior half this deepens to a heavier dirty brown. The central coating of the anterior portion thins toward the edge, becoming an inflammatory red, with elevated and redder papillae. The appearance of the tongue was noted earlier than any other symptom.

Mello-Leitao,⁹⁴ studying the refractometric index of the blood in measles, believes it to be of value in differentiating that disease from rubella.

Complications and Sequelae.—Wilson⁹⁵ studied 2,000 cases of measles in the Contagious Hospital at Ellis Island and concludes that cross infection, especially that of diphtheria, is the most serious event that can occur in measles. Suppurative otitis media, although the most frequent complication, is not of grave import when properly treated. Bronchopneumonia complicated about 10 per cent. of all measles cases, being but little influenced by weather conditions in the frequency of its occurrence or its fatality. The fatality of measles complicated by bronchopneumonia was 58 per cent., but this varied in an exceedingly erratic manner and without marked relation to the total case fatality of the disease. Wilson came to the conclusion that the incidence rate of bronchopneumonia as a complication, rather than its case mortality,

93. Herrman: Am. Jour. Obst., 1915, **72**, 739.

94. Gardner: Am. Jour. Clin. Med., 1916, **23**, 925.

95. Wilson: Med. Rec., New York; 1916, **84**, 756.

appeared to be an index to the severity of any particular outbreak of measles.

Dupuy⁹⁶ finds that 10 per cent. of measles patients suffer from middle ear abscesses. He gives a few whiffs of ethyl chlorid in children over 2 years old in order to perform a technically perfect tympanotomy. Whenever the ears are suspected, Dupuy opens both drums. He found every drum to be off-colored, slightly hyperemic, during the last epidemic. This shows how easily the integrity of the middle ear becomes disturbed during an attack of measles.

Case Reports.—Secher⁹⁷ reports that thirteen out of thirty-one children affected with measles suffered from an enteritis which he believes was the result of the localization of the disease in the bowels. In seven the enteritis was quite severe and two of the children died. Bacteriologic findings were negative. Eaton and Woods⁹⁸ report two cases of measles complicated by whooping cough, death occurring in one, possibly from pneumonia. Opdyke⁹⁹ saw measles in a 7-year-old girl, which followed an attack of whooping cough and influenza and which was complicated by a fatal mastoiditis and meningitis. Moore¹⁰⁰ describes a case of acute generalized tuberculosis with left oculomotor paralysis occurring after an attack of measles.

Winter¹⁰¹ reports two cases of measles exanthemata in infants 16 and 18 days old, respectively, in whom there was a history of typical prodromata a day before. Winter comments that since we know that the prodromal and incubation stage of measles is thirteen to sixteen days, and only exceptionally longer, one has to admit that in both instances the infection occurred in extra-uterine life, in the first case most probably on the first day of life, and in the second, most probably on the first to third day. This observation disproves the contention that the new-born are immune to exogenous infections.

Sainton¹⁰² speaks of a case of severe inflammation of the anterior half of the tongue (hemiglossitis) complicating measles.

Mortality.—Boudreau¹⁰³ shows that measles causes about twice the number of deaths every year in Ohio that scarlet fever does, and that the case-fatality rate is very high under 5 years, being as high as 25 per cent., and very low over 10 years, less than 1 per cent.

96. Dupuy: New Orleans Med. and Surg. Jour., 1917, **69**, 741.

97. Secher: Berl. klin. Wchnschr., 1916, **53**, 250.

98. Eaton and Woods: Arch. Pediat., 1916, **33**, 513.

99. Opdyke: New York Med. Jour., 1916, **103**, 986.

100. Moore: Dublin Jour. Med. Sc., 1916, **141**, 174.

101. Winter: Jahrb. f. Kinderh., 1915, **81**, 465.

102. Sainton: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 709.

103. Boudreau: Ohio State Med. Jour., 1916, **12**, 104.

The death rate for 1915 in the registration area for measles was 5.4 per 100,000 of population, the lowest since 1900.¹⁰⁴

Treatment.—Longin¹⁰⁵ treated more than 100 cases of malignant measles with intravenous injections of colloidal gold. The mortality among these patients ranged from 3 to 5 per cent., whereas the mortality for the epidemic as a whole was 12 per cent. Longin believes that the striking results, especially the rapid subsidence of the temperature and pulse and the continuation of the great improvement, are the result of the medication.

Place¹⁰⁶ protests against the unhygienic manner in which measles patients are often treated and urges that the medical profession substitute for the irrational and often harmful ideas of management a sensible, rational and scientific handling of the disease. He believes that disinfection is of no value and that isolation is helpful only if it can be applied thoroughly.

Experimenting with ethylhydrocuprein, Hirschfelder and Schultz¹⁰⁷ obtained negative results in scarlet fever, but in measles the effect seemed more promising. Eleven treated cases averaged 4.3 days, while the average of ten untreated cases was 7.9 days. This would indicate that the drug is worthy of further trial.

SCARLET FEVER

Epidemiology and Prophylaxis.—Hubbard¹⁰⁸ thinks that there is no such thing as controlling scarlet fever, at least in New York City. Isolation as formerly practiced in that city was not satisfactory, so trained nurses were substituted for medical inspectors, the former combining social welfare work with the duties of establishing isolation, and the change has been highly successful. In New York City they regard the patient as the original source of infection and concentrate their efforts there. The most frequent carriers of infection, they think, are the patient, persons coming into contact with the latter, and lastly, the patient's surroundings, the bedding, room, clothing, etc. This being accepted, control must be exercised by isolation continued until every possible danger for the public has passed.

From his recent experiences during an epidemic of scarlet fever in Amsterdam, Heijermans¹⁰⁹ wonders whether isolation and placarding are the best means of prophylaxis in scarlet fever. They do not seem to check the disease and apparently are not effective as at present

104. Jour. Am. Med. Assn., 1916, **67**, 1457.

105. Longin: Med. Press and Circ., 1916, **102**, 184.

106. Place: Boston Med. and Surg. Jour., 1916, **175**, 704.

107. Hirschfelder and Schultz: AM. JOUR. DIS. CHILD., 1916, **11**, 360.

108. Hubbard: Med. Rec., New York, 1916, **84**, 490.

109. Heijermans: Nederl. Tijdschr. v. Geneesk., 1916, **2**, 1719.

applied. He advocates notification of cases, but no placarding of houses. Heijermans is not in favor of hospitalization, believing that it is better to keep the children at home, reserving the hospital for the cases of exceptional severity. Many children are sent there who do not have the disease, a positive diagnosis being doubtful. Further, there is no evidence that institutional treatment wards off complications.

Ekholm¹¹⁰ found that in the last twenty years, 50 per cent. of the buildings in his city have had no cases of scarlet fever in them. In other buildings the disease occurred again and again. There were twenty-three return cases following dismissal of 724 patients from the hospital as cured. Ekholm makes the significant statement that walking cases without eruption are probably responsible in many instances for the spread of the disease.

Boudreau¹⁰⁸ outlines the prevention of scarlet fever as depending on the following: (1) skilful and conscientious physicians; (2) well organized health departments; (3) contagious disease hospitals; (4) public health nurses to visit cases; (5) physical supervision of school-children; (6) cooperation of an enlightened public; (7) supervision of the milk supply.

Chesley¹¹¹ says that one of the essentials in the control of the disease is the follow-up and supervision of exposed persons, as well as inspection of schoolchildren, the follow-up of absentees and the tracing of the source of infection. In his opinion desquamation is no objection to terminating isolation. Chesley thinks that hospitalization or isolation in care of a trained attendant is preferable to house isolation. Ker¹¹² pays no attention to scarlet desquamation and regards a minimum detention period of four weeks as an indication of a welcome change in responsible medical opinion, and hopes that at the present moment, when all are asked to be economical, health authorities will take advantage of this change in order to reduce hospital expenditures.

Chapin¹¹³ believes that the hospital as a factor in exterminating scarlet fever has been disappointing. Even the usual methods of home isolation are not of great value. The disease is still very prevalent and is only slowly decreasing. No doubt more intensive work in ferreting out the mild cases as sources of infection would do much toward reducing the prevalence of the disease, especially in small communities. Chapin emphasizes that the ideal to be strived for is the isolation of more cases, not more isolation of the cases. Too much should not be attempted in the isolation of the case in the family. If 40 or 50 per

110. Ekholm: *Finska Lakar. Handl.*, 1915, **57**, 5.

111. Chesley: *Am. Jour. Pub. Health*, 1916, **6**, 234.

112. Ker: *Lancet*, London, 1916, **1**, 481.

113. Chapin: *Boston Med. and Surg. Jour.*, 1916, **175**, 715.

cent. of the cases could be isolated in hospitals, the full value of the latter would be secured.

Ringeling,¹¹⁴ studying the cases of scarlet fever in Amsterdam, concludes that not much can be anticipated from hospital treatment of the disease in general prophylaxis, especially since healthy bacillus carriers cannot be isolated. He attributes the low mortality to prompt hospitalization, quoting London statistics to the effect that in 1890, 42.8 per cent. of the cases were in hospitals, with a mortality of 5.6 per cent.; in 1910, 85.6 per cent. were hospitalized, with a mortality of 2 per cent.

Lewis¹¹⁵ thinks that he has practically abolished recurrent cases of scarlet fever, made secondary cases infrequent and lessened reported cases, by isolating the carriers of convalescence and the carriers previously having had the disease. In his opinion the control of scarlet fever will be found to lie in the supervision of those who have previously had the disease, at and during those periods when with recurrent infections they again show the buccal-pharyngeal signs of the disease.

In a later communication Lewis¹¹⁶ indicates that throat cultures in scarlet fever frequently give the same aid as in diphtheria. He finds that a certain streptococcus, morphologically, gives reliable data, and he uses the appearance of this streptococcus as a cause for search for either acute cases or carriers in an endeavor to control the disease. He thinks that over a period of one and half years the method has proved its value most exactly.

Broadbent¹¹⁷ reports a case of what he regards as a scarlet fever carrier.

Etiology.—Not a great deal of experimental work on the bacteriology of scarlet fever has been done in the past two years, but two entirely different organisms have been brought forward as the cause of the disease. Mallory and Medlar¹¹⁸ found a gram-positive bacillus which they think is the causative organism, while Mair¹¹⁹ of Cambridge reports a diplococcus as responsible.

Mallory and Medlar found their gram-positive bacillus postmortem in the crypts of the tonsils, in the exudation on the tonsils, and in almost pure culture in slight depressions and erosions in the squamous epithelium covering the tonsils, the pillars of the fauces, the soft palate, including the palate and the root of the tongue. Along the surface and in the upper part of the exudation in the trachea similar masses

114. Ringeling: *Nederl. Tijdschr. v. Geneesk.*, 1916, **2**, 1874.

115. Lewis: *Boston Med. and Surg. Jour.*, 1916, **175**, 683.

116. Lewis: *Boston Med. and Surg. Jour.*, 1917, **176**, 170.

117. Broadbent: *Lancet*, London, 1916, **2**, 121.

118. Mallory and Medlar: *Jour. Med. Research*, 1916, **34**, 127.

119. Mair: *Jour. Path. and Bacteriol.*, 1916, **20**, 366.

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are found, as well as along the basement membrane of the same region. They were also found in the bronchioles and alveoli of a bronchopneumonic lung. The organism was found in the tissues of eight persons dying of the disease and in smears and cultures from the tonsils, soft palate, pharynx and nasopharynx of sixty patients. The bacillus is strongly gram-positive, in culture being slightly smaller than the diphtheria bacillus and varying from coccus-like to large bacillary forms. Pairs and short chains are common, while in the water of condensation long chains are found. The organisms isolated are facultative aerobes, growing best on serum glycerin. Mallory and Medlar¹²⁰ conclude that it is reasonable to infer that scarlet fever may be due to a strongly gram-positive bacillus which is less virulent than *B. diphtheriae* and which infects practically the same localities. Fibrin formation is absent or slight, and on this account primary gross lesions are inconspicuous. There is no membrane formation unless due to secondary streptococcus invasion. The toxin of this organism causes necrosis of the epithelial layers and occasionally of the deeper tissues, leading to an exudate of serum and polymorphonuclear leukocytes. In uncomplicated fulminant cases the causative organism is present in large numbers in the lesions in the respiratory tract up to the time of death, but in milder cases they seem to die out quickly, so that by the second or third day after the eruption they are impossible of demonstration. Under certain conditions they may persist for weeks, the patient becoming a scarlet fever carrier.

Secondary infection with streptococci is common and death is occasionally due to them rather than to the bacillus of scarlet fever. The eruption and the nephritis are both probably of toxic origin.

The organism believed by Mair to be responsible for scarlet fever is a diplococcus, which can be demonstrated, according to him, in the throats of scarlet fever patients during the first week of the disease in 87 per cent. of cases. It disappears usually about the fifth week of convalescence, but in some patients persists much longer.

In monkeys the diplococcus produces a disease resembling scarlet fever, but it has little tendency to produce septicemia. Mair found it confined to the region of primary invasion, usually the throat, and there it produces toxins which are poured into the blood stream. Scarlatinal arthritis is a feature common to the disease in both man and monkeys. No definite evidence of nephritis has yet been found in the monkey, nor does the rash occur.

Additional evidence in support of the diplococcal theory is found in the fact that complement fixation reactions occur with much greater frequency and with greater intensity in scarlet fever than in control

120. Mallory and Medlar: Jour. Med. Research, 1916, **35**, 209.

cases. This observation is against the view that the diplococcus is a secondary invader.

Schleissner¹²¹ experimented with streptococci, blowing a twenty-four-hour culture of scarlet fever streptococci into the noses and mouths of monkeys. This was followed by fever, angina, enanthem and strawberry tongue, and after ten days there was desquamation in large flakes. Attempts at reinfection was unsuccessful, so there seemed to be an immunity developed. Attempts to infect with germ-free bouillon cultures were unsuccessful.

These facts make it highly probable, in Schleissner's opinion, that this scarlet fever streptococcus is the specific cause of the disease.

Watson¹²² calls attention to the close similarity of complications and sequelae in rheumatic fever, scarlet fever and malignant endocarditis, and suggests that there is a common factor in their cause. The blood changes in these three diseases are the same, a polymorphonuclear leukocytosis in each. Watson feels justified in concluding that in all these cases there is a septic infection of the lymphoid tissues in the region of Peyer's patches. Further than that, he believes that every symptom of scarlet fever points to an acute intestinal catarrh, fatal in malignant cases and productive of intense irritation in those of ordinary severity.

Serum Reactions.—Dick and Dick,¹²³ by the use of complement fixation tests, were unable to demonstrate any specific scarlatinal virus or antigen in the blood serum or in extracts of spleen or lymph glands. Fixation tests with throat mucus as antigen gave in one instance a weak fixation of complement with the serum of a convalescent scarlet fever patient. They found that the toxicity of human blood serum for guinea-pigs is increased during the acute stage of scarlet fever. Positive Wassermann reactions in scarlet fever obtained with the acetone-insoluble portion of alcoholic heart extract are strongly suggestive of syphilis.

On the supposition that the weakly positive complement-fixation reaction, using mucus from a scarlatinal angina as antigen, was due to a micro-organism capable of growth, cultures were made of the mucus and tested as to antigenic properties by means of complement fixation and intracutaneous tests.¹²⁴ These cultures showed the presence of an antigen which reacted with scarlatinal serum to fix complement in more than half the cases tested, whereas controls gave positive reactions in over one-third of the cases tested. Comparing the antigenic property of streptococci with that of the mixed cultures

121. Schleissner: *Jahrb. f. Kinderh.*, 1915, **82**, 225.

122. Watson: *Glasgow Med. Jour.*, 1915, **84**, 401.

123. Dick and Dick: *Jour. Infect. Dis.*, 1916, **19**, 175.

124. Dick and Dick: *Jour. Infect. Dis.*, 1916, **19**, 638.

of the preceding experiment, the results obtained would indicate that no antigenic properties need be assumed in any of the antigens prepared from scarlatinal throats, other than that of the streptococci present.

Cutaneous tests were also carried out, using a heat-killed culture of mucus from scarlatinal throats, with a pure culture of a hemolytic streptococcus from a fatal scarlatinal angina and a milk and whey culture from an ordinary tonsillitis. Any specificity comparable to the tuberculin cutaneous test could not be demonstrated.

Symptoms.—Berg¹²⁵ classifies the severe scarlet fever cases into the toxic, the toxic hemorrhagic and the septic. The prognosis in the septic type is better than in the toxic, but true hemorrhagic cases are invariably fatal. Berg believes that the so-called scarlatina accompanying burns, surgical injuries and the puerperal states is not scarlet fever, but a symptom of sepsis.

Ostrovsky¹²⁶ found that in the initial stage of scarlet fever there is retention of chlorids and that from the tenth to the twentieth day the amount eliminated rises in waves.

Gauss¹²⁷ studied the spinal fluids from fifty cases of scarlet fever and "associated exanthems," and found them all sterile, with the exception of four contaminations. The pressure varied with the mental and physical attitude of the patient. The cell count varied from 1 to 29 cells per cubic centimeter, averaging 8 cells.

Traumatic and Pseudoscarlet Fever.—Korach¹²⁸ reports the case of a physician who casually excoriated one hand and was then exposed to scarlet fever. In forty-eight hours he developed a typical scarlet fever lymphangitis and by the third day he presented the general symptoms of scarlet fever with the rash.

Frankel¹²⁹ has observed among children numerous cases which, although resembling scarlet fever, differ from it essentially, and etiologically seem to be more nearly related to influenza. The onset is usually sudden, with elevation of temperature and a scarlatiniform rash, but the course is milder and the rash paler, more evanescent and is followed by more minute desquamation. Frankel hopes to focus attention on these cases and urges their investigation by those equipped for research work.

Lasalle¹³⁰ reports a case of pseudoscarlatina of toxic origin, probably due to copper sulphate.

125. Berg: Am. Jour. Obst., 1915, **72**, 1074.

126. Ostrovsky: Russk. Vrach, 1916, **15**, 7.

127. Gauss: Jour. Am. Med. Assn., 1917, **68**, 779.

128. Korach: Deutsch. med. Wchnschr., 1917, **43**, 12.

129. Frankel: New York Med. Jour., 1916, **104**, 799.

130. Lasalle: Arch. de méd. d. enf., 1916, **19**, 91.

Morbidity and Mortality.—Dublin¹³¹ studied the complete records of 1,153 cases of scarlet fever. Nearly 82 per cent. were among children between 2 and 10 years of age, the greatest predisposition being found between 3 and 7 years of age. The death rate was 7.8 per cent. for the series, 15.5 per cent. occurring during the second year. Ninety-two per cent. of all deaths were in children under 10 years of age.

Tracing the 1,063 patients who survived, and who were under observation for an average period of 3.4 years, he found that only eighteen deaths occurred, whereas 18.6 deaths were expected. The actual mortality, then, was 97 per cent. of the expected, as compared with a mortality in those surviving an attack of typhoid fever twice as great as was to be expected.

Of the eighteen deaths, three patients died of endocarditis, five of respiratory diseases and four from tuberculosis. There were no deaths from kidney disease. Generally speaking, the death rate for colored children was about one-fourth that of white children.

Donnally,¹³² in a study of the morbidity and fatality of scarlet fever based on several million cases, concludes that periodicity in the appearance of epidemics cannot be made out; that a decline in morbidity cannot be generally demonstrated; that the sexes as a whole show equal susceptibility; that about two children out of three between 3 and 8 years of age contract scarlet fever if exposed to the disease in their homes, if they have not previously had it; that it appears to be a milder affection than formerly, but that epidemics may vary greatly in virulence and have been attended by greater fatality in some places than in others.

Ostheimer¹³³ says that 1,072 cases of scarlet fever were reported from Philadelphia in 1915, less than one-third the number reported in 1913. This is a morbidity rate of 63.7 per 100,000 as compared with 208 in 1913. Of the patients, 74.6 per cent. were treated in hospitals, the death rate for the entire city being 2.4 per cent.

The death rate from scarlet fever in the registration area¹³⁴ in 1915 was 3.6 per 100,000 of population, the lowest since 1900.

Case Reports.—Several cases of interest are reported by different observers. Iglauer¹³⁵ reports a rare complication, a case of esophageal stenosis, which he dilated by a method of his own, the latter being fully described; Lynah,¹³⁶ a case of osteomyelitis of the sinuses of the

131. Dublin: Jour. Am. Med. Assn., 1916, **66**, 1667.

132. Donnally: AM. JOUR. DIS. CHILD., 1916, **12**, 205.

133. Ostheimer: Am. Jour. Pub. Health, 1916, **6**, 1104.

134. Jour. Am. Med. Assn., 1916, **67**, 1457.

135. Iglauer: Lancet-Clinic, 1916, **115**, 289.

136. Lynah: Laryngoscope, 1917, **27**, 176.

nose, with apparent recovery; Cooke¹³⁷ reports six cases of hyperthyroidism occurring after mild scarlet fever, all in males, within a period of four months, and all in the same ward. He suggests that a microbic infection was responsible. Lortat-Jacob and Oppenheim¹³⁸ believe that a comparison of the symptoms shown by their patient with those of postscarlatinal paresis confirms the assumption that cerebral arteritis is responsible for the chronic infectious hemiplegia in such conditions. Miller¹³⁹ speaks of a case apparently exhibiting measles and scarlet fever simultaneously, while three other children in the family had measles alone. Smith¹⁴⁰ cites what he believes was an instance of three attacks of scarlet fever in the same child within a year. Squibbs¹⁴¹ tells of a relapsing scarlet with general glandular enlargement.

Nobécourt, Jurie des Camiers and Tournier¹⁴² report several cases of scarlet fever complicated by articular rheumatism, endocarditis and pericarditis. The same observers¹⁴³ saw two cases of phlebitis during the course of scarlatina. Ramond and Chambas¹⁴⁴ report icterus as occurring in 8 per cent. of 131 cases of scarlet fever seen by them. Creyx¹⁴⁵ saw a case with a combined scarlatinal and scarlatiniform rash.

Clough¹⁴⁶ reports a very interesting instance of postscarlatinal anuria in a child of 7, in whom, with one exception, the daily output of urine was never more than 4 ounces over a period of thirty-four days. Only 91 ounces were passed from March 23 to May 7. Only once were two casts found in the urine, and no albumin was present at any time. No sort of treatment had any effect on the condition, but the child at the time of the report was in perfect health.

Ramond and Schultz¹⁴⁷ call attention to neuralgias seen during the early days of scarlet fever, while Hutinel¹⁴⁸ discusses at length the pneumonias of scarlatina. Florand and Merklan¹⁴⁹ remark on the fre-

137. Cooke: Jour. Roy. Army Med. Corps, 1916, **27**, 114.

138. Lortat-Jacob and Oppenheim: Progrès méd., 1916, **31**, 213.

139. Miller: Arch. Pediat., 1917, **34**, 138.

140. Smith: Brit. Med. Jour., 1915, **1**, 1003.

141. Squibbs: Med. Times, 1915, **43**, 745.

142. Nobécourt, Jurie des Camiers and Tournier: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 779.

143. Nobécourt, Jurie des Camiers and Tournier: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 807.

144. Ramond and Chambas: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 770.

145. Creyx: Jour. de méd. de Bordeaux, 1917, **88**, 30.

146. Clough: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 367.

147. Ramond and Schultz: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 298.

148. Hutinel: Arch. de méd. d. enf., 1916, **19**, 57.

149. Florand and Merklan: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 985.

quency of rheumatism in scarlet fever and state that it is of the chronic arthralgic type. It frequently undergoes spontaneous cure. The heart should frequently be examined during scarlatina, as cardiac involvement frequently occurs, endocarditis with murmurs, symptoms of passing myocarditis, etc.

Liddell and Tangye¹⁵⁰ cite a case of supposed intra-uterine scarlet fever. Four of five children in a family developed the disease, the mother being confined eleven days after the removal of the children to the hospital. After a thorough washing, which removed all traces of lanugo, the trunk and limbs of the new-born infant were found to be desquamating freely. This lasted for several days and the urine showed distinct traces of albumin. The mother had been rather unwell during the last week of pregnancy, but had no sore throat or rash and her temperature was normal.

Haeggstrom's¹⁵¹ patient developed otitis media during scarlet fever, necessitating an operation on the second day for mastoiditis. Six days later there was a profuse hemorrhage from which the child died. Necropsy showed the side wall of the sigmoid sinus to be completely eroded. Twenty-five similar cases were found in the literature.

Wilson¹⁵² is impressed with the mental apathy which children in the Contagious Disease Hospital at Ellis Island often exhibit during convalescence from scarlet fever and measles. He reports a case showing catatonic postures.

Prophylactic Vaccination.—Di Cristina¹⁵³ prepared a vaccine with 15 c.c. of convalescent serum and 10 gm. of desquamated shreds and scales, adding 0.8 per cent. phenol and 1 c.c. of guinea-pig complement, incubating for fifteen hours at 37 C. One c.c. of this vaccine was given subcutaneously every second day, from 0.75 to 4 c.c. in all. By the second or third injection the specific deviation of complement occurred.

The children thus treated had all been casually exposed to scarlet fever, but none of them developed the disease. Encouraged by this success, he left some of the vaccinated children in the scarlet fever ward for several days. Other children had been placed in this same ward by mistake. They were vaccinated after twenty-four hours' exposure and then allowed to sleep with patients in the eruptive stage and in the desquamative stage, but none of the vaccinated children developed the disease, even when kept in bed with scarlet fever sufferers for several days. Di Cristina declares that there is something in the scales which confers immunity on healthy children, the immunity

150. Liddell and Tangye: *Brit. Med. Jour.*, 1916, **2**, 389.

151. Haeggstrom: *Hygiea*, 1916, **79**, 58.

152. Wilson: *Jour. Abnormal Psychol.*, 1916, **11**, 123.

153. Di Cristina: *Pediatrics*, 1916, **67**, 385.

thus induced being rendered manifest by the deviation of complement test.

Serum Treatment.—Additional reported cases confirm Reiss and Hertz¹⁵⁴ opinion as to the great value of convalescent serum in scarlet fever, which in many cases saves life. They found it necessary to give the serum intravenously and in large doses, at least 50 c.c. in children and 100 c.c. in adults, though the gravity of the case and the day of the disease should be taken into consideration. Cases that were injected as late as the fourth or fifth day gave no prompt results.

Concerning normal serum, there is no doubt that occasionally action similar to that of convalescent serum was observed. The action of Moser's serum was very similar to that of convalescent serum. Normal horse serum seems to have no effect on scarlet fever, while the danger of serum disease speaks for the use of serum from convalescents.

The indication for the use of the serum is the appearance of scarlatina gravissima, when in a few days a picture of severe scarlet fever intoxication occurs, especially with a small, irregular pulse, cyanosis, stupor or delirium. Those cases in which a serious picture develops, due to secondary infection, are unsuitable for this treatment; for example, necrotic angina, suppurative cervical adenitis, lung complications, endocarditis, uremia, etc. The sooner the injection is made the better are the results, after the fourth or fifth day the serum rarely having any effect.

Zingher¹⁵⁵ treated severe forms of scarlet fever with intramuscular injections of fresh human blood, either convalescent or normal. In a number in whom the outlook was doubtful if not poor, 6 or 8 ounces of blood seemed to have a life-saving effect and encourages him to recommend the treatment in the severer forms of the disease. In nine septic or toxic cases treated with 3 to 8 ounces of whole blood obtained from three to six weeks convalescents, there was, in some, a critical drop in temperature within twelve to twenty-four hours, together with a distinct improvement in the pulse and general condition. Two patients died from the advanced septic state.

Zingher¹⁵⁶ favors the use of whole blood rather than serum, because of the loss of 60 per cent. of the blood with the latter method. The treatment is easily carried out, is quite harmless, and can be done by the general practitioner. He believes that the rational element in the use of convalescent serum is quite apparent, while that in the use of fresh normal blood is found in the clinical observations of its empirical value, and also in the great nutritive value of homologous blood, its marked stimulating properties, and its well-known antibody content.

154. Reiss and Hertz: *München, med. Wchnschr.*, 1915, **62**, 1177.

155. Zingher: *Med. Rec.*, New York, 1915, **88**, 335.

156. Zingher: *Jour. Am. Med. Assn.*, 1915, **65**, 875.

A year later Zingher,¹⁵⁷ in a third communication, reports further experience with the method. He used fresh whole blood from a convalescent donor injected into the patient's muscles, either directly or after citrating. Fourteen patients with toxic scarlet fever, in whom the prognosis was doubtful or absolutely poor, were injected in amounts varying from 75 to 250 c.c., depending on the age of the patient. Of the fourteen patients injected, four died. In the remaining ten there appeared to be a distinctly favorable influence on the course of the disease. In those not complicated by a streptococcus exudate or cervical adenitis, there was a distinct critical drop in temperature. Even in the septic forms of the disease there was seen an improvement in the general condition. Larger quantities, 8 to 10 ounces, of fresh blood seemed to have a distinctly beneficial effect on the disease, especially when repeated in four or five days.

Other Forms of Treatment.—Hirschfelder and Schultz,¹⁵⁷ experimenting with ethylhydrocuprein, obtained negative results.

Love¹⁵⁸ advocates the inclusion of autogenous vaccine therapy in the routine treatment of scarlatinal otorrhea and other more trifling complications. He believes that it greatly lessens the duration of the discharges and appears to effect a rapid and permanent cure without detriment to the patient.

Hutinel¹⁵⁹ describes malignant scarlet fever and says that through the use of epinephrin, the mortality of this form of the disease has been reduced 50 per cent.

Ramond and Schultz¹⁶⁰ point out that the many analogies between scarlet fever and acute rheumatism are confirmed by the benefits derived from salicylate medication. They give 6 gm. or more a day, keeping it up until the fever, etc., have subsided, usually within three days, but to be safe, the drug is given two days longer. On the fifteenth day it is resumed again, the dose reduced 1 gm. a day. This wards off complications, which are so liable to develop between the fifteenth and the twentieth days, especially tonsillitis and nephritis. The mortality under this treatment dropped to 0.25 per cent., and complications were exceptional.

In another report Ramond¹⁶¹ speaks of the good effects of sodium salicylate in scarlet fever, while Esmein¹⁶² believes salicylic acid to be of value, even against nephritis.

157. Zingher: New York State Jour. Med., 1916, **16**, 112.

158. Love: Jour. State Med., 1915, **23**, 202.

159. Hutinel: Med. Press and Circ., 1915, **100**, 166.

160. Ramond and Schultz: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **32**, 866.

161. Ramond: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 869.

162. Esmein: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 140.

DIPHTHERIA

Epidemiology.—Crum¹⁶³ says that diphtheria is perhaps as prevalent today from the viewpoint of its worldwide distribution as it has ever been, there being reason to believe that it is still spreading geographically and tending to become endemic in the remoter sections of the earth. Some practical means of removing or effectually opposing the underlying conditions favorable to the spread of the disease must be sought for. It must be admitted that many of the possibly very important underlying conditions favoring its spread are not well understood.

Despite all that is known regarding diphtheria, the incidence of the disease, says Perkins,¹⁶⁴ has not materially decreased. Why such lack of success? Because in diphtheria we have a disease the virus of which is transmitted by very direct contact through the personal element, a factor difficult of control, in contradistinction to our ability to control inanimate objects which are responsible chiefly for the spread of typhoid fever. There will be no very material decrease in the incidence of diphtheria until public opinion will permit health departments to establish the percentage and distribution of diphtheria nonimmunes.

Control of Epidemics.—Brooks¹⁶⁵ reports the control of a long standing epidemic of diphtheria in a city of 54,000 inhabitants, the activities including culturing of school children and contacts, control of carriers, close supervision and enforcement of rational isolation, hospitalization when necessary, and the seeking out of unreported cases. Brooks concludes that, generally speaking, the communicable disease rate of any municipality indicates the degree of effectiveness of health activities, and he feels there is serious need of stimulation of civic consciousness and of education to the need of intelligent cooperation, if health is to be protected.

Benz¹⁶⁶ believes that from his experience diphtheria can be held to a minimum in the schools only by continued and repeated cultures of all suspected cases. In order to control a localized epidemic of diphtheria in a school, Stovall¹⁶⁷ immunized all who had a positive Schick reaction and isolated those with positive cultures. No further cases developed.

Lewis¹⁶⁸ first endeavored to control diphtheria outbreaks by controlling contacts and convalescents bacteriologically. He found, how-

163. Crum: Am. Jour. Pub. Health, 1917, **7**, 445.

164. Perkins: Ohio State Med. Jour., 1917, **13**, 89.

165. Brooks: New York State Jour. Med., 1917, **17**, 295.

166. Benz: Penn. Med. Jour., 1917, **20**, 395.

167. Stovall: Jour. Am. Med. Assn., 1917, **68**, 1089.

168. Lewis: Jour. Am. Med. Assn., 1916, **66**, 1535.

ever, that not a single case could be traced to infection from those in whom physical examination gave a negative, and culture a positive, result. As a result, no contacts were isolated if the pharynx was normal, even though cultures were positive. Combined with a neighborhood survey for missed cases and carriers, the procedure resulted in a notable decrease of diphtheria.

Moffitt¹⁶⁹ takes exception to the statement that in 95 per cent. of cases no Klebs-Loeffler bacilli were found after two weeks, and in 98 per cent. none after four weeks. He found that but 68 per cent. were negative at the end of three weeks and 76 per cent. at the end of four weeks. For that reason he believes that isolation should not be terminated until negative cultures have been obtained.

To prevent the occurrence of diphtheria in hospital wards Adams and Leech¹⁷⁰ would keep new cases in detention for five days, after having nose and throat cultures taken. Infants should be kept isolated from children of the run-about age and visiting should be restricted to adult patients.

Virulence of Diphtheria Bacilli.—Studying cultures of diphtheria bacilli for acid production with various carbohydrates in order to determine the practical value of these tests in aiding differentiation among the members of the diphtheria group, Kolmer and Moshage¹⁷¹ found that acid production tests are not sufficiently regular to be depended on in determining the harmfulness of a given culture. They are of most value in the study of the solid varieties of diphtheria-like bacilli; cultures proving nonvirulent for guinea-pigs and producing no acid with sugars, are classified as Hofmann's type; nonvirulent cultures producing acid with one or more sugars are regarded as nonvirulent diphtheria bacilli.

The same workers¹⁷² studied the question of the possible relationship between the toxin and the carbohydrate-splitting process, concluding that carbohydrate fermentation by diphtheria bacilli is dependent on secretory enzymic products of the organism, but is independent of the soluble toxin. The carbohydrate-splitting products are most likely, however, to be formed by toxin-producing bacilli.

Cary¹⁷³ also worked on acid production in carbohydrates and found that there was a maximal acid production for each strain of diphtheria bacilli in various carbohydrates, the rapidity of production varying with the greater relative exposure to air, the time varying not only with the carbohydrate, but with the different strains. Cary could not

169. Moffitt: Penn. Med. Jour., 1915, **19**, 23.

170. Adams and Leech: Am. Jour. Obst., 1916, **74**, 556.

171. Kolmer and Moshage: Jour. Infect. Dis., 1916, **19**, 19.

172. Kolmer and Moshage: Jour. Infect. Dis., 1916, **19**, 28.

173. Cary: Jour. Infect. Dis., 1917, **20**, 244.

demonstrate any constant relationship between virulence and the fermentation reactions. The number of organisms necessary for a fatal result is a good indication of virulence, but gives no idea of the toxicity of the strain.

Weaver¹⁷⁴ states that diphtheria bacilli from patients with diphtheria and carriers who have been in contact with such patients are practically always virulent, and usually remain so up to the time of disappearance, even after a long time. He urges that carriers be isolated until the organisms disappear or are proved to be nonvirulent.

Kolmer, Woody and Moshage¹⁷⁵ find virulence tests to be useful in the management of diphtheria carriers, especially from the standpoint of the duration of isolation. The tests must be sufficiently delicate to detect low degrees of virulence and must be economical and as speedy as consistent with specificity and delicacy. The best results were obtained with the subcutaneous injection of 4 c.c. of a good twenty-four-hour culture of diphtheria bacilli on Loeffler's serum. In 1,054 tests barred bacilli were found of equal virulence with the granular types, the latter being virulent in about 70 per cent. of cultures. Long solid bacilli were virulent in about 42 per cent. of cases, while short solid bacilli were uniformly nonvirulent.

Zingher and Soletsky¹⁷⁶ describe a new and economical method for testing the virulence of diphtheria bacilli, and Zingher¹⁷⁷ presents in detail an intradermal test for estimating in an economical way small amounts of antitoxin. The method is easily carried out, though it requires for accuracy a uniform technic.

Diphtheroids.—Fox¹⁷⁸ reviews the literature on the subject of diphtheroids and discusses it at length. There is nothing to show the origin of the nonvirulent members of that group, but that they are degraded forms is suggested. Fox¹⁷⁹ conducted a series of experiments in the attempt to cause mutation or degradation of diphtheria bacilli by the influence of lymph tissue and blood, but was not successful. The morphology remained quite constant except for a tendency in late generations to grow in long, clubbed, mycelial forms and these morphologic changes have probably given some observers the basis for the assumption of mutation.

Complement Fixation.—Levy¹⁸⁰ showed that fixation of complement by the serum of persons from a diphtheria environment occurs,

174. Weaver: Jour. Infect. Dis., 1917, **20**, 125.

175. Kolmer, Woody and Moshage: AM. JOUR. DIS. CHILD., 1916, **11**, 257.

176. Zingher and Soletsky: Jour. Infect. Dis., 1915, **17**, 454.

177. Zingher: Jour. Infect. Dis., 1916, **19**, 557.

178. Fox: Jour. Med. Research, 1915, **32**, 325.

179. Fox: Jour. Med. Research, 1915, **32**, 309.

180. Levy: Ann. de méd., 1915, **2**, 597.

but it is seen more constantly and positively in those who have had diphtheria. They were evidently rendered immune by the presence of a bacillary focus, the products of the activity of the latter causing an ample supply of antibodies.

Culture Technic—Shimer¹⁸¹ says that the advantages of the potassium tellurate medium for diphtheria cultures over the Loeffler blood serum method are an increased number of positives, a lessened number of bacteria in smears, a decrease of almost half in the time necessary to examine slides and an enormous lessening of the work necessary to obtain pure cultures.

Gehrmann¹⁸² found that a gain in time can be expected when immediate incubation of diphtheria cultures is practiced. In his experience the body heat may be used for their incubation with perfect satisfaction.

Experimental Diphtheria Toxemia.—Bailey¹⁸³ administered large doses of toxin intravenously to the rabbit and found that it produced a pronounced vascular and parenchymatous degeneration in the kidney. Emge¹⁸⁴ found that a toxemia produced in guinea-pigs in such a way as to simulate the course of human diphtheria toxemia does not lead to changes in the thyroid gland to the same degree as has been observed in the human thyroid gland in fatal diphtheria. The changes seen are not sufficiently marked to permit the conclusion that this gland has a detoxicating action in experimental diphtheritic toxemia.

Diphtheria in the First Year of Life.—Analyzing 2,600 consecutive cases of diphtheria, Rolleston¹⁸⁵ found that less than 1 per cent. were under 1 year of age. Sixty-five per cent. of these showed nasal involvement, with or without diphtheria somewhere else, as compared with 25.6 per cent. of the total with nasal infection. Thirty per cent. were purely nasal, as compared with 1.5 per cent. of the total cases. The mortality was high, 45 per cent., as compared with 7.3 per cent. mortality among the whole number.

Laryngo-Tracheo-Bronchial Diphtheria.—Lynah¹⁸⁶ presents an excellent discussion of diphtheria of the tracheobronchial tree. He thinks the condition is commoner than is believed and that in the majority of cases the infection travels from below upward. As an aid to treatment the membrane should be mechanically removed through a bronchoscope by means of a small suction tube attached to a vacuum

181. Shimer: Jour. Bacteriol., 1916, **1**, 111.

182. Gehrmann: Am. Jour. Pub. Health, 1915, **5**, 1031.

183. Bailey: Jour. Exper. Med., 1917, **25**, 109.

184. Emge: Jour. Infect. Dis., 1915, **17**, 369.

185. Rolleston: AM. JOUR. DIS. CHILD., 1916, **12**, 47.

186. Lynah: Laryngoscope, 1916, **26**, 158.

pump. After removal of the membrane the tracheobronchi are intubated with long tracheobronchial tubes. Thirty-eight cases are reported¹⁸⁷ with fourteen deaths.

Rolleston¹⁸⁸ reviews the subject of laryngeal diphtheria in adults and adds four cases of his own. He calls attention to the rarity of the condition, to its grave prognosis, to the absence or late onset of severe dyspnea, to the inefficacy of serum or other treatment and to the sudden character of the termination.

Smith¹⁸⁹ reports a case of primary tracheal or bronchial diphtheria, with recovery, a cast being coughed up. The diagnosis was confirmed bacteriologically. Lynah¹⁸⁶ remarks that he has yet to see a case of laryngeal diphtheria relieved by tracheotomy in which intubation failed.

Nasal Diphtheria.—In 3,000 cases Rolleston¹⁹⁰ found only fifty-five, or 1.5 per cent., of isolated nasal diphtherias, as compared with 260, or 20.6 per cent., in which nasal diphtheria was associated with an angina.

Ochsenius¹⁹¹ found 88 per cent. of nasal diphtherias to be confined to one nostril. The course was always favorable, the general health being but slightly impaired.

Extra-Oral Diphtheria.—Emge¹⁹² reports a case of primary diphtheria of the skin. Billings¹⁹³ says that there are only twenty-five cases of primary cutaneous diphtheria on record, and reports two cases, both on the fingers. Rolleston¹⁹⁴ reports a whitlow involving the left index, middle and ring fingers of two and a half months' duration, in the discharge from which diphtheria bacilli were found, and which healed within a week after the administration of 8,000 units of antitoxin.

Ceconi¹⁹⁵ saw a primary diphtheria of the vulva. Da Roche¹⁹⁶ tells of a case of primary localization of diphtheria on the conjunctiva. Egyedi¹⁹⁷ and Gaillard¹⁹⁸ both saw diphtheria complicate a primary syphilitic sore, one on the vulva, the other on the lip.

An interesting case of diphtheria of an abdominal gallbladder wound is related by Bristol¹⁹⁹ who calls attention to the fact that

187. Lynah: Laryngoscope, 1916, **26**, 1193.

188. Rolleston: Clin. Jour., 1916, **45**, 389.

189. Smith: Brit. Med. Jour., 1915, **2**, 57.

190. Rolleston: Brit. Jour. Child. Dis., 1917, **14**, 21.

191. Ochsenius: München. med. Wchnschr., 1916, **63**, 1450.

192. Emge: Jour. Am. Med. Assn., 1915, **65**, 529.

193. Billings: Ann. Surg., 1915, **62**, 343.

194. Rolleston: Brit. Jour. Dermat., 1916, **28**, 110.

195. Ceconi: Boston Med. and Surg. Jour., 1916, **174**, 838.

196. Da Roche: Brazil-méd., 1916, **30**, 219.

197. Egyedi: Deutsch. med. Wchnschr., 1916, **42**, 1354.

198. Gaillard: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, **39**, 1036.

199. Bristol: Am. Jour. Pub. Health, 1915, **5**, 838.

because of the exposed nature, long duration and failure to recognize wound and skin diphtheria, it is especially dangerous as a source of the disease in general.

Vinsonhaler²⁰⁰ reports a case of diphtheria primarily involving the sinuses, mastoid and middle ear.

Case Reports.—Knack²⁰¹ describes the occurrence of eight tonsillar abscesses among 500 cases of diphtheria, in six of which the causative organism proved to be *Streptococcus hemolyticus*. Gunson²⁰² reports a case of gangrene of the leg following diphtheria, the popliteal artery being found completely occluded by a thrombus. Only sixteen cases have been reported up to 1916. Lynah²⁰³ reports a case of a safetypin in the larynx with a perilaryngeal abscess, which was diagnosed and treated as a laryngeal diphtheria. Skillern²⁰⁴ tells of a diphtheritic membrane in the right lung simulating a foreign body, which was diagnosed and removed through the bronchoscope.

Downie,²⁰⁵ Mason,²⁰⁶ Daley and McCormack²⁰⁷ and Mills and Mendelson²⁰⁸ all report cases of postdiphtheritic paralysis. Barabas²⁰⁹ found that in eight children out of sixteen with postdiphtheritic paralysis, sensitiveness of the skin to pain was greatly if not entirely abolished, while the sensations of heat, cold and touch were apparently not impaired. Ravaut and Krolunitsky²¹⁰ report a case of generalized diphtheritic paralysis with a meningeal reaction, evidenced by the presence of a positive albumin test and a lymphocytosis in the spinal fluid.

Gerson²¹¹ tells of two cases of myasthenic bulbar paralysis, both in chronic diphtheria carriers, and he asks if this coincidence may not possibly explain the etiology of this affection. Gunson²¹² found a crossed reflex present in 76 per cent. of cases of diphtheria. He believes that this indicates involvement of the cord in a larger number of cases than is generally recognized, and that it suggests that the motor weakness, ataxia and loss of knee jerks may be largely dependent on a central lesion of a toxic inflammatory character.

200. Vinsonhaler: South. Med. Jour., 1916, **9**, 839.

201. Knack: Ztschr. f. Hyg. u. Infektionskr., 1915, **80**, 163.

202. Gunson: Brit. Jour. Child. Dis., 1916, **13**, 237.

203. Lynah: Laryngoscope, 1917, **27**, 93.

204. Skillern: Laryngoscope, 1917, **27**, 100.

205. Downie: Practitioner, 1915, **45**, 55.

206. Mason: Ophth. Rec., 1916, **25**, 140.

207. Daley and McCormack: Lancet, London, 1916, **1**, 915.

208. Mills and Mendelson: New York Med. Jour., 1916, **103**, 780.

209. Barabas: Jahrb. f. Kinderh., 1916, **82**, 476.

210. Ravaut and Krolunitsky: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, **40**, 913.

211. Gerson: Berl. klin. Wchnschr., 1916, **53**, 1364.

212. Gunson: Rev. Neurol. and Psychiat., 1915, **13**, 317.

Rolleston and Gunson²¹³ describe a case of extensive occlusion of the cerebral arteries. They analyzed eighty cases of diphtheritic hemiplegia which they were able to collect from the literature, embolism appearing to be the most common cause of that variety of lesion.

Carriers.—Weaver¹⁷⁴ says that observation has emphasized the fact that persistent carriage of diphtheria bacilli usually depends on some local condition, such as diseased tonsils, adenoids or sinuses, and while these carriers are less dangerous as spreaders of infection than recent cases of diphtheria, yet they must be considered as potential agents for dissemination of disease and isolated until the organisms have been shown to be nonvirulent.

Ruediger²¹⁴ thinks the carrier of great importance in transmitting the disease and advocates their isolation, unless the bacilli prove to be nonvirulent. He does not believe that it is possible to pick out carriers by mere inspection of the throat, as recently advocated by Lewis.¹⁶⁸

Perkins, Miller and Ruh²¹⁵ studied diphtheria in Cleveland, with special reference to carriers. In their experience the organisms of the Hofmann type have never proved virulent, and they believe that the most satisfactory attitude towards diphtheria is that which eliminates all diphtheria-like forms as etiologic factors in the disease.

Studying the phagocytic power of the blood of diphtheria carriers, Tunncliff²¹⁶ found it to be increased, but noted at the same time that the nose and throat may contain large numbers of leukocytes not engaged in phagocytosis. Efforts to increase the activity of these leukocytes by the use of normal serum, leukocytic suspensions, calcium chlorid, sodium salicylate, lactic acid, and magnesium chlorid, were unsuccessful, although dilute solutions of these substances are found to promote phagocytosis in vitro.

Treatment of Carriers.—Rappaport²¹⁷ reiterates that when properly applied, kaolin by its adsorptive power mechanically removes bacteria with which it comes in contact. Stress is laid on the method of application, the kaolin being first thoroughly dried, then passed through a fine flour sieve before being evenly distributed over the surface to be treated. Its action is interfered with by local pathologic conditions, removal of the tonsils and adenoids being advocated when the organisms persist unduly long in spite of kaolin.

Bell²¹⁸ suggests trying the kaolin treatment first because of its simplicity, especially in private homes, but the desired results are not

213. Rolleston and Gunson: *Rev. Neurol. and Psychiat.*, 1915, **13**, 373.

214. Ruediger: *Illinois Med. Jour.*, 1916, **30**, 255.

215: Perkins, Miller and Ruh: *Jour Infect. Dis.*, 1916, **18**, 607.

216. Tunncliff: *Jour. Infect. Dis.*, 1916, **19**, 97.

217. Rappaport: *Jour. Am. Med. Assn.*, 1916, **66**, 943.

218. Bell: *Arch. Pediat.*, 1916, **33**, 836.

accomplished as quickly as with the staphylococcus spray, which, when properly applied from a laboratory and clinical standpoint, is a safe and successful method of combating diphtheria carriers.

McKay²¹⁹ reports that from an experience with thirty-six carriers treated with a bouillon culture of lactic acid bacilli there is very little shortening in the period of isolation.

Many other methods of treatment have been tried by various observers. Ott and Roy²²⁰ report a series of seventeen carriers treated by the application of acidum carbolicum iodatum (N. F.), sixteen of which had negative cultures within eleven days. No bad results were noticed, though a thin escharotic membrane was formed at the site of application, which disappeared in forty-eight hours, leaving the throat red for a few days.

Labbe and Canat²²¹ believe they obtained favorable results from the insufflation of powder made from serum of horses previously injected with heat-killed diphtheria bacilli. No organisms were to be found in thirty-five cases after an average of twenty-four days of treatment, while the intervals averaged over forty days in a group treated with the ordinary antiseptic measures. Beattie, Lewis and Gee²²² experimented with hypochlorous solution electrically produced from hypertonic salt solution as a disinfectant in these cases. In a series of fifty-nine which were bacteriologically positive, they were able to reduce the average time in hospital from 23.2 days in patients not treated to 16.4 days in those treated. Thacker²²³ cocaineizes the throat, then paints the parts with 50 per cent. silver nitrate. The nostrils are plugged with gauze soaked in 1 in 10 ichthyol in glycerin. Two applications cleared up eight diphtheria carriers. Ewart²²⁴ suggests the instillation of jasmine oil into the nostrils as a means of ridding carriers of the organisms.

Lynch²²⁵ believes in the efficacy of vaccines, but thinks tonsillectomy the ideal procedure. Love²²⁶ treated seven persistent carriers with vaccines of killed diphtheria bacilli, without much apparent effect.

Several other observers unite in advocating the removal of tonsils and adenoids to clear up persistent carriers. Wherry²²⁷ recommends

219. McKay: *Am. Jour. Pub. Health*, 1915, **5**, 982.

220. Ott and Roy: *Jour. Am. Med. Assn.*, 1916, **66**, 800.

221. Labbe and Canat: *Paris méd.*, 1917, **7**, 9.

222. Beattie, Lewis and Gee: *Brit. Med. Jour.*, 1917, **1**, 256.

223. Thacker: *Brit. Med. Jour.*, 1916, **1**, 374.

224. Ewart: *Brit. Med. Jour.*, 1915, **2**, 854.

225. Lynch: *New Orleans Med. and Surg. Jour.*, 1916, **68**, 782.

226. Love: *New Orleans Med. and Surg. Jour.*, 1916, **68**, 778.

227. Wherry: *Western Med. Rev.*, 1916, **21**, 15.

it. Friedberg²²⁸ removed them without any general ill effects. Cowie²²⁹ found the method to be the most efficient of any. Rabinoff²³⁰ says that the results with various other methods were disappointing, with the exception of those obtained with fuller's earth in adults, removal of tonsils and adenoids being recommended when other methods fail. Ruh, Miller and Perkins²³¹ conclude that the period of isolation for carriers can be materially shortened by the removal of these structures and no adverse effects were ever experienced.

Meador²³² asserts that pathologic changes in the epithelium might be observed long after clinical manifestations had disappeared, but that these foci are not apparent to the unaided eye. While removal of the tonsils was followed by a report of negative cultures, still there is no data to show that foci on a large part of the mucosa might not still be infected. In his experience immunization with diphtheria bacilli vaccines was not a fruitful field of endeavor, inasmuch as he had been unable to demonstrate any trace of antibodies for these organisms.

Brown²³³ sectioned the tonsils from seven diphtheria carriers and demonstrated gram-positive, beaded bacilli in great numbers in six. The one case which showed no gram-positive bacilli continued to give positive cultures, so that it is reasonable to infer that in this case the bacteria were multiplying in some other place than the tonsils.

Schick Test.—More has been written on the Schick test than on any other one phase of diphtheria, the practical value of the reaction having been amply demonstrated by many observers.

Park and Zingher²³⁴ emphasize the great reliability of the test. A negative reaction obtained after the age of 2 or 3 years indicates that the individual is protected, probably indefinitely, against the disease. The great majority of reactions are true reactions and indicate an absence of antitoxin in the blood. The test is of value in clearing up clinically doubtful diagnoses of diphtheria and by its use the unnecessary sensitization of about one-half of exposed individuals may be avoided.

Zingher²³⁵ found it to help in the diagnosis of nasal diphtheria, and thinks that the results obtained in families seem to point to other causes in addition to bacterial infection with virulent diphtheria bacilli as determining factors in the production of natural antitoxin.

228. Friedberg: *Jour. Am. Med. Assn.*, 1916, **66**, 810.

229. Cowie: *Jour. Mich. Med. Soc.*, 1917, **16**, 72.

230. Rabinoff: *Jour. Am. Med. Assn.*, 1916, **67**, 1722.

231. Ruh, Miller and Perkins: *Jour. Am. Med. Assn.*, 1916, **66**, 941.

232. Meador: *Med. Rec.*, New York, 1915, **88**, 127.

233. Brown: *Jour. Infect. Dis.*, 1916, **19**, 565.

234. Park and Zingher: *Am. Jour. Pub. Health*, 1916, **6**, 431.

235. Zingher: *Am. Jour. Obst.*, 1915, **72**, 735.

In a later communication Zingher²³⁶ says that the accuracy of the results obtained with the test will depend not only on the toxin, but also on the care with which the test is made and on the interpretation of the reaction. A positive reaction should be considered as indicating a lack of immunity, unless the pseudoreaction can be eliminated by a control test. The results with the test obtained in 2,700 normal children show that from 17 to 32 per cent. between the ages of 2 and 16 years give a positive reaction and are probably susceptible to diphtheria.

Somewhat later the same worker²³⁷ found the test to be positive between 1 and 4 years of age in about 32 per cent. of normal children, in a slightly larger proportion of cases of measles, in twice as many scarlet fever cases and nearly three times as many cases of poliomyelitis. He believes that susceptibility to one of the less communicable diseases, like poliomyelitis, indicates that the child is more apt to be susceptible to other infectious diseases. The presence or absence of natural immunity, as shown by the Schick test, could be profitably studied in its relation to the mendelian law.

Weaver and Rappaport²³⁸ tested 194 healthy young adults with the Schick reaction, and of these 52.6 per cent. gave negative results. They believe that it seems reasonable to assume that mild and unrecognized attacks of diphtheria are responsible for the increasing proportion of persons immune to diphtheria with increasing age. They found the test to be of value in the diagnosis of carriers who are sick from other anginas than diphtheria, Weaver¹⁷⁴ showing that all carriers gave negative reactions. In scarlet fever 33.3 per cent. gave positive results. These workers find that a limited antitoxin production is probably to be expected in some instances after the reaction.

Kolmer²³⁹ advocates delaying the reading of the toxin reaction until forty-eight hours have elapsed in order to allow slight false reactions to disappear, although in the presence of an outbreak it is best to regard all reactions of erythema and edema measuring a quarter of an inch or more in diameter as positive. As a practical procedure the test has two main applications: to detect those susceptible to diphtheria, and as an aid in the diagnosis of the disease.

Moffett and Conrad²⁴⁰ studied the test in 455 children up to 14 years of age, concluding that it is of value in differentiating doubtful membranes in the throat; that it tests the efficacy of antitoxin immunization; that in institutional epidemics it is of value in lessening the

236. Zingher: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 269.

237. Zingher: *AM. JOUR. DIS. CHILD.*, 1917, **13**, 247.

238. Weaver and Rappaport: *Jour. Am. Med. Assn.*, 1916, **66**, 1448.

239. Kolmer: *Penn. Med. Jour.*, 1916, **19**, 333.

240. Moffett and Conrad: *Jour. Am. Med. Assn.*, 1915, **65**, 1011.

amount of antitoxin used by differentiating the susceptibles from the nonsusceptibles.

Greenebaum and Hettler,²⁴¹ Sewall,²⁴² Stovall,²⁴³ Linenthal and Rubin,²⁴⁴ Veeder,²⁴⁵ Levinson,²⁴⁶ Schiller,²⁴⁷ Earle,²⁴⁸ Sprenger²⁴⁹ and others,²⁵⁰ are agreed on the value of the test in differentiating doubtful membranes and as a prompt, economic and satisfactory method of controlling epidemics of diphtheria by a determination of susceptibility. Schiller thinks susceptibility is a family characteristic, but Sprenger disagrees. The latter found that carriers gave a negative reaction.

Earle thinks the test is unsatisfactory in the colored race, but Wright²⁵¹ states that the reaction is as clear cut in negroes as it is in whites. Bullen²⁵² retested 100 children after eleven months and found that 18 per cent. of those who gave a positive reaction in May, 1914, showed no reaction in April, 1915, while fifteen who gave no reaction when first tested showed more or less strongly marked reactions at the time of the second test.

In one series of sixty normal children Levinson and Blatt²⁵³ found 78.13 per cent. were negative to the toxin test. In a series of fifty-five afflicted with diseases other than diphtheria or tuberculosis, 61.8 per cent. were negative. Of thirty-three children suspected of having tuberculosis, the Schick test seemed to have no effect on a simultaneous von Pirquet reaction, or vice versa. In thirty-eight tuberculous children, sixteen were positive, but the results bore no relation to the reaction obtained from tuberculin treatment.

Shaw and Youland²⁵⁴ found that 47 per cent. of sixty-six children under 1 year of age and 58.6 per cent. of twenty-nine children in their second year gave positive reactions. They recommend that when virulent diphtheria bacilli are found in infants who have no antitoxin in their tissue, a careful examination for diphtheritic rhinitis should be made, as they had five cases in which it was overlooked clinically.

Cowie²⁵⁵ found that successive intradermal injections of very dilute

241. Greenebaum and Hettler: *Lancet-Clinic*, 1916, **116**, 389.

242. Sewall: *Jour. Mich. Med. Soc.*, 1916, **15**, 290.

243. Stovall: *Jour. Am. Med. Assn.*, 1916, **66**, 804.

244. Linenthal and Rubin: *Boston Med. and Surg. Jour.*, 1915, **173**, 427.

245. Veeder: *Internat. Clin.*, 1916, **3**, 180.

246. Levinson: *Illinois Med. Jour.*, 1915, **28**, 40.

247. Schiller: *Wisconsin Med. Jour.*, 1916, **14**, 453.

248. Earle: *Western Med. Rev.*, 1916, **21**, 24.

249. Sprenger: *Illinois Med. Jour.*, 1916, **29**, 447.

250. Bullen: *Am. Jour. Obst.*, 1915, **72**, 735.

251. Wright: *Jour. Infect. Dis.*, 1917, **21**, 265.

252. Bullen: *New York State Jour. Med.*, 1916, **16**, 208.

253. Levinson and Blatt: *Arch. Diagnosis*, 1915, **8**, 201.

254. Shaw and Youland: *Am. Jour. Obst.*, 1916, **74**, 558.

255. Cowie: *AM. JOUR. DIS. CHILD.*, 1916, **12**, 266.

solutions of diphtheria toxin (0.00001 c.c. L+ dose), given at intervals varying from five to twelve days, provoke the formation of antibodies, and in those already exhibiting a certain degree of immunity, brings about a definite immunity as recognized by the intradermal test. The degree of immunity, however, cannot be compared with the results obtained by the use of toxin-antitoxin mixtures. An early primary reaction of ordinary degree indicates absence or low degree of immunity. A late appearing primary reaction indicates a greater degree of immunity than an early reaction. The development of immunity induced by small successive doses of toxin may be recognized by a hastening in the time of appearance of the reaction and a diminution in the size of the lesion. A primary reacting case which does not change its character after repeated injections may be considered to be without protecting bodies.

Hitchens and Tingley²⁵⁶ found that the Schick test made intrapleurally was, to a considerable degree, anticipative of the antitoxin productiveness of horses.

Technic of the Test.—Koplik and Unger²⁵⁷ believed that if the toxin injected approximated one-fiftieth the maximum lethal dose rather than accurately equaled that amount, all the indications of the test would be met. They, therefore, devised a needle so constructed that when it is inserted its full length, after being dipped into undiluted toxin, the amount of the latter carried in approximated one-fiftieth the maximum lethal dose.

Weaver and Rappaport²⁵⁸ slightly modified the technic of the test, thrusting the needle into the skin at right angles to the surface to a depth of one-eighth inch. The direction is then changed so that if carried forward the needle would emerge one-half inch from the point of entrance. This method is less painful, requires less time than the old and obviates the escape of fluid.

Litterer²⁵⁸ calls attention to the readiness with which diphtheria toxin deteriorates even in its native state. It must be of definite strength, else the test would be fallacious. He has made an effort to preserve a toxin so that it can be rendered stable for a reasonable period when subjected to room temperature. The most practicable method consisted in introducing dried toxin into a vial with 2 c.c. of sterile liquid albolene or toluol and immersing the whole in cold water. This rendered the toxin quite stable for six weeks at room temperature or for more than eight months at 48 F.

256. Hitchens and Tingley: Jour. Immunol., 1917, **2**, 395.

257. Koplik and Unger: Jour. Am. Med. Assn., 1916, **66**, 1195.

258. Litterer: Southern Med. Jour., 1917, **10**, 103.

To overcome the difficulties in popularizing the test, Zingher²⁵⁹ presents a simplified outfit for the distribution of the toxin.²⁶⁰ In working with the test, Perkins, Miller and Ruh²¹⁵ come to the conclusion, in agreement with other observers, that smaller amounts of fluid should be injected, that a small needle should be used, and that freshly sterilized salt solution gives a smaller proportion of false reactions than when old salt solution is used.

Pseudoreaction.—Zingher²⁶¹ says that the pseudoreaction of the toxin test is caused by the protein substance of the diphtheria bacillus which is present in the solution used for the test, and may be seen in those who have enough natural antitoxin to render them immune to diphtheria. Park²⁶² found that about 3 per cent. of cases tested gave a positive reaction. Levinson²⁴⁶ says that no test should be considered positive unless there is induration measuring at least 0.5 by 0.2 cm., and a reaction persisting at least five days.

Kolmer and Moshage²⁶³ made a study of the pseudoreaction and conclude that it is advisable, when doing Schick tests, to use as highly potent toxin as possible in order to dilute the protein constituents of the bouillon. The toxin should be so diluted that only 0.05 or 0.1 c.c. need be given, and not more than 0.25 per cent. of tricresol should be present. It is also better to read the reaction after forty-eight hours than after twenty-four hours. The use of bouillon controls aids in detecting these pseudoreactions.

Experimenting with the Schick reaction, Bessau and Schwenke²⁶⁴ found an element in the bouillon which was not neutralizable by antitoxin and was apparently not modified by heat. They believe that in all probability this heat-resisting substance is a preformed toxin (endotoxin) in the diphtheria bacillus. The reaction to this endotoxin cannot be regarded as an index to the antitoxic content of the blood and hence of the immunity to diphtheria. It seems possible that the question of immunity to diphtheria, which seems to have been settled, may have to be studied anew.

Kolmer and Moshage²⁶⁵ injected intracutaneously a polyvalent antigen of washed, neutralized and heat-killed diphtheria bacilli, which they call diphtherin, and observed an allergic skin reaction following in about 70 per cent. of children and 35 per cent. of adults. This reaction has no value as an index of immunity and is of practical inter-

259. Zingher: Med. Rec., New York, 1916, **84**, 667.

260. Zingher: Jour. Am. Med. Assn., 1916, **65**, 329.

261. Zingher: Jour. Am. Med. Assn., 1916, **66**, 1617.

262. Park: Med. Rec., New York, 1915, **88**, 505.

263. Kolmer and Moshage: Jour. Am. Med. Assn., 1915, **65**, 144.

264. Bessau and Schwenke: Monatschr. f. Kinderh., 1915, **13**, 397.

265. Kolmer and Moshage: AM. JOUR. DIS. CHILD., 1916, **12**, 316.

est mainly from the point of view that it may be mistaken for a positive Schick reaction. Kolmer²⁶⁶ further says that hypersensitiveness to diphtheria protein cannot be taken as an index to diphtheria immunity and that anaphylactic states bear no constant relation to the presence or absence of such antibodies as may be detected by experiments in vitro.

Toxin-Antitoxin Mixtures.—Park and Zingher²⁶⁷ have done considerable work with toxin-antitoxin immunization. They find that individuals who, before treatment, gave a negative Schick reaction are probably immune for life and therefore it is not necessary to inject them, when exposed, with either antitoxin or toxin-antitoxin. If a longer protection is desired, those who are not immune may be given both antitoxin and toxin-antitoxin. For general prophylaxis in schools and communities, excluding immediate contacts, a mixture of toxin-antitoxin alone (from 85 to 90 per cent. of the L+ dose of toxin to each unit of antitoxin) or toxin-antitoxin plus a vaccine of killed diphtheria bacilli is recommended. The dose is 1 c.c. of toxin-antitoxin and 1,000,000,000 bacteria injected subcutaneously and repeated three times at intervals of six or seven days. Sufficient time has not elapsed to judge of the value of the addition of diphtheria bacilli. The early and late results of active immunization may be determined with the Schick test. In another communication they²⁶⁸ say that while toxin-antitoxin injections cannot be depended on to prevent diphtheria in the presence of immediate danger of infection, because of the slow development of immunity in the majority of cases, yet the injection is of value in rendering a community or school population immune from the danger of future infection up to a period of possibly several years.

Later in the year they²⁶⁹ presented statistics based on over 1,000 cases that had been actively immunized. No harmful after-effects were noted. The retest with the Schick reaction showed that only 30 to 40 per cent. became immune within three weeks after the first injection, about 50 per cent. by the fourth week, 70 to 80 per cent. by the sixth week, and 90 to 95 per cent. by the eighth to twelfth week. In a group studied over a period of one and one half years, it was found that immunity persisted at least that time. From their results Park and Zingher conclude that it is advisable to immunize children soon after the first year of life in order to confer protection against diphtheria at a time when the disease is most dangerous. An immune child population could thus be developed with the result that fresh clinical cases

266. Kolmer: Jour. Immunol., 1916, **67**, 1333.

267. Park and Zingher: Jour. Am. Med. Assn., 1915, **65**, 2216.

268. Park and Zingher: Proc. New York Path. Soc., 1915, **15**, 110.

269. Park and Zingher: Med. Rec., New York, 1916, **90**, 741.

would be prevented and the bacillus carrier would probably soon disappear as a hygienic factor in the community.

Park²⁷⁰ noticed that those who have natural antitoxin respond rapidly to the injection of toxin-antitoxin mixtures, but in those without antitoxin no appreciable response occurs for fourteen days, and in 50 per cent. not for four weeks. The full response is not seen until the third month. Only 95 per cent. of susceptibles become immune. Park believes the procedure has its most practical value in institutions.

Bullen²⁸⁰ injected forty-one children having positive Schick tests with toxin-antitoxin mixtures. When tested later, all but eight still had markedly positive reactions.

Lynch²²⁵ urges that children be immunized by the von Behring method before they are admitted to the public schools, unless the Schick test is negative.

Busson and Lowenstein²⁷¹ tried the effects of toxin-antitoxin mixtures on animals. In using mixtures that were kept in the icebox for one or two months, a change occurred that permitted doubly neutralized mixtures to produce the same immunity as exactly neutralized or under-neutralized mixtures. They obtained no better results by reinjection of the mixture.

Opitz²⁷² declares that even one antitoxic unit per cubic centimeter of serum does not protect against diphtheria, therefore in active immunization one should strive for as high an antitoxic content as possible. Excretion of passively introduced antibodies occurs independently of the day of the disease, of the gravity of the disease, and of the size of the dose of serum, occurring more or less rapidly in the weeks following injection.

Linenthal and Rubin²⁴⁴ gave thirty-six children 750 units of antitoxin each. This produced an immunity which lasted not over four weeks in half the children, eight weeks in several, and in six children it persisted after five months.

Cultural Diagnosis.—Walthall²⁷³ showed that the pharynx may be negative for Klebs-Loeffler bacilli, but that they may be present in the nose or larynx, and that one tonsil may give positive cultures while all other portions of the mucous membrane are negative. Geiger, Kelly and Bathgate²⁷⁴ lay stress on the importance of nose cultures. In a series of cultures those from the nose gave 42.2 per cent. positive and from the throat 7.9 per cent. positive.

270. Park: Boston Med. and Surg. Jour., 1916, **175**, 721.

271. Busson and Lowenstein: Ztschr. f. exper. Path. u. Therap., 1915, **17**, 289.

272. Opitz: Deutsch. med. Wchnschr., 1915, **41**, 914.

273. Walthall: AM. JOUR. DIS. CHILD., 1916, **12**, 149.

274. Geiger, Kelly and Bathgate: Jour. Am. Med. Assn., 1916, **66**, 645.

Clark's²⁷⁵ statistics from various countries emphasize the vital importance of commencing treatment at the earliest possible moment, early diagnosis being the important factor. Seidel²⁷⁶ says that a twenty-hour culture should not be regarded as sufficient for a negative diagnosis, but a forty-four-hour culture should be examined. Neff²⁷⁷ urges that direct smears be taken from patients with a membrane in order to hasten the diagnosis. Then it is not necessary to wait for the result of a culture. He²⁷⁸ believes the mortality is much too high, and urges that an earlier diagnosis be made or that antitoxin be administered without waiting for cultural confirmation.

Morbidity and Mortality.—Crum¹⁸⁸ conservatively estimates that not fewer than 250,000 lives are at present saved annually from the ravages of diphtheria through the use of antitoxin and other improved methods of diagnosis and treatment. The disease, however, still causes more deaths than whooping cough, measles or scarlet fever, the annual number of deaths being 17,000.

Baginsky²⁷⁹ reports on 525 cases of diphtheria in one year with a mortality of 15.6 per cent. with the use of antitoxin, in contrast with a mortality of 48.21 per cent. in the year before serum was used. Of those treated on the first day the mortality was 1.07 per cent., on the sixth day, 19.2 per cent. and on the seventh day, 27.2 per cent. The death rate in the Alexandra Hospital, according to Cushing and Murphy,²⁸⁰ was 7.5 per cent. over a period of ten years. Of 205 patients intubated or tracheotomized, fifty-five died, a rate of 27 per cent., but in 1915 only 16 per cent. of intubated patients died. The mortality is always raised by the septic cases in which the patients first improve, then die of cardiac failure, and by hemorrhagic cases, twelve of which occurred in the above mentioned series, and in which all patients died.

Reiche²⁸¹ contrasts the diphtheria incidence and mortality of four communities, two of which were prosperous and two very much lower in the social scale. The percentage of mortality in the prosperous communities was 4.13 as against 15.8 in the other.

The death rate from diphtheria and croup in 1915 in the registration area²⁸² was 10,544, or 15.7 per 100,000, having fallen from 43.3 in 1900. This decline of more than 60 per cent. is relatively greater than that shown by any other important cause of death except typhoid fever.

275. Clark: Brazil-méd., 1916, **30**, 417.

276. Seidel: München. med. Wchnschr., 1915, **62**, 1209.

277. Neff: Jour. Am. Med. Assn., 1915, **65**, 585.

278. Neff: Jour. Kansas Med. Soc., 1916, **16**, 142.

279. Baginsky: Berl. klin. Wchnschr., 1915, **52**, 1268.

280. Cushing and Murphy: Canada Med. Assn. Jour., 1916, **6**, 817.

281. Reiche: Berl. klin. Wchnschr., 1915, **52**, 643.

282. Jour. Am. Med. Assn., 1916, **67**, 1457.

Hitchcock²⁸³ investigated seventy-three deaths from diphtheria in the Connecticut Valley and found that the physician's first visit was not made until the fourth day or later in 53.5 per cent. of the cases, while 36.9 per cent. of patients died on or before the fifth day. He believes that any case which is clinically suspicious enough to warrant taking a culture for diagnostic purposes is suspicious enough to warrant the administration of antitoxin without waiting to hear from the culture.

Prophylactic Serum Treatment.—Cushing and Murphy²⁸⁰ found the danger of infection to attendants greater from diphtheria than from any other disease treated in the hospital. No attempt was ever made to immunize the attendants with prophylactic injections of serum, as it was felt that the benefits of the resulting brief immunity were not in proportion to the discomfort and disability of the serum reaction. Better quarters and better care of the attendants has apparently materially decreased the number of secondary cases among them.

Weaver and Rappaport²⁸⁸ give every nurse in the Durand Hospital who shows a positive Schick reaction, 1,000 units of antitoxin. Every month they are retested and are reimmunized when a positive reaction again appears.

In reply to a questionnaire sent to Spanish physicians by Alvarez,²⁸⁴ inquiring as to their experience with antitoxin, they were unanimous in asserting that the fear of by-effects should not prevent its use for curative purposes. Its administration as a preventive occasioned considerable difference of opinion, the majority agreeing, however, that its use in hospitals, asylums, etc., is justified when the disease is epidemic.

Antitoxin Dosage and Methods of Administration.—Bell²⁸⁵ believes it strange that after the lapse of twenty-six years since the discovery of antitoxin it should be necessary to herald its virtues or urge its use. While there are few physicians who do not use it at all, there are many who do not use it properly. He urges the use of sufficiently large doses and much prefers the intramuscular and intravenous methods of administration. There is no limit to the dose, so far as danger is concerned, the only thing to fear is that it may be too small. Practically, Bell finds that the intravenous method is very simple, one of the veins at the bend of the elbow being preferred and an ordinary antitoxin syringe used. Woody²⁷⁷ advocates very large doses, the average given by him being 23,800 units. He feels, however, that the advantage of the intravenous method of administration are overbalanced by the difficulties of its use, particularly in general practice and in children, and he favors the intramuscular route as having many advantages over the subcutaneous method.

283. Hitchcock: Boston Med. and Surg. Jour., 1916, **175**, 718.

284. Alvarez: Siglo méd., 1916, **63**, 630.

285. Bell: Ohio State Med. Jour., 1916, **12**, 618.

Others (see Footnotes 277, 286, 287, 288, 289) urge that large doses be given at the first injection, Stammel²⁸⁶ advising that croup cases which do not clear up within two or three hours be treated as diphtheria, and that antitoxin be administered without waiting for the result of cultures. Many (see Footnotes 290, 291, 292, 287, 280) are strongly in favor of the intravenous method, especially in the laryngeal form of the disease. Ferguson²⁸⁷ says that he has not seen a patient die who has lived twenty-four hours after antitoxin was given. Dupaquier²⁹² believes that when the technic of the intravenous method is perfected it will be the routine manner of giving antitoxin. Lynah,¹⁸⁷ on the other hand, prefers the intramuscular route.

Antitoxin Standardization.—MacConkey²⁹³ examined thirty-one samples of antitoxin which had been in commerce for an average period of two and a half years, and found that it showed an average loss of 23 per cent. or about 10 per cent. a year. The author concludes that unless one knows how the serum has been stored, the time expiration label means nothing and may lead to a false sense of security.

The Committee on Standard Methods of Preparing Diphtheria Antitoxin²⁹⁴ supplement their report of four years ago, giving in detail Banzhof's latest method of refining and concentrating serum.

Heinemann²⁹⁵ succeeded by a combination of well-known methods and persistent repetition of certain details in producing a serum with a higher concentration than obtained with former methods. Because nontoxic proteins are eliminated the solids of the new preparation need not be higher than 18 to 20 per cent. This serum is of attractive appearance, water clear for at least one year and its consistence is such that it is easily discharged through a hypodermic syringe. The antitoxic globulins realized by this method are easily soluble and dialysis is consequently rapid. Nonantitoxic protein being eliminated in large measure, serum disease, so far as present observations go, is greatly reduced.

Treatment of Laryngeal Diphtheria.—Bell²⁹⁶ reports the use of a tube for thirty-one days. This was an apparently hopelessly sick 1-year-old baby, which completely recovered. The very distressing

286. Stammel: *Lancet-Clinic*, 1915, **113**, 655.

287. Ferguson: *Illinois Med. Jour.*, 1915, **28**, 401.

288. Delearde: *Bull. de l'Acad. de méd.*, Paris, 1916, **76**, 173.

289. Capitan: *Bull. de l'Acad. de méd.*, Paris, 1916, **75**, 653.

290. Bell: *Lancet-Clinic*, 1915, **114**, 104.

291. Greene: *South. Med. Jour.*, 1917, **10**, 164.

292. Dupaquier: *New Orleans Med. and Surg. Jour.*, 1915, **68**, 145.

293. MacConkey: *Brit. Med. Jour.*, 1917, **1**, 10.

294. Heinemann, Anderson, Park, Hitchens and Pease: *Am. Jour. Pub. Health*, 1916, **6**, 751.

295. Heinemann: *Jour. Infect. Dis.*, 1916, **19**, 433.

296. Bell: *Arch. Pediat.*, 1916, **33**, 161.

cough was relieved by dropping 2 per cent. cocain solution into the tracheal tube at intervals. A tracheotomy had had to be performed also.

Local Methods of Treatment.—Local treatment of diphtheria with tribrombetanaphthol has the advantage, according to Leshke,²⁹⁷ of causing the membrane to disappear sooner, of favorably affecting the clinical course, and of rapidly developing freedom from bacilli, thus preventing the spread of infection.

Treatment of Post-Diphtheritic Paralysis.—Passler²⁹⁸ noted rapid improvement of a postdiphtheritic paralysis and eventual recovery within a month, under large doses of antitoxin. Maggiore²⁹⁹ treated a boy suffering from postdiphtheritic paralysis with injections of a vaccine made with an emulsion of inactivated diphtheria bacilli in diphtheria antitoxin. The paralysis began to improve at once. Maggiore regards the factors involved as those on which active immunity is based.

Weaver and Rappaport³⁰⁰ tested three cases of postdiphtheritic paralysis with the Schick test. In one the reaction was positive. After administration of antitoxin the advancing paralysis stopped abruptly and recovery rapidly followed.

Serum Sickness.—With a view to ascertaining the frequency and severity of the symptoms of serum sickness, Sturtevant³⁰⁰ studied 500 consecutive cases receiving serum. He found that of 422 patients receiving one injection, 20 per cent. showed symptoms. The larger the amount of serum, the larger the number reacting. Most reactions occurred from the fifth to the ninth day, though they occurred as early as the first and as late as the seventeenth day. The symptoms were a rash, nausea and vomiting, albuminuria and edema occasionally, either alone or together, and joint symptoms in about 14 per cent. of reacting cases.

Cushing and Murphy³⁰⁰ have no record of true anaphylactic shock and death in the Alexandria Hospital, though serum is given both intramuscularly and intravenously. They are convinced that the latter method has a distinct future.

Hassler³⁰¹ reports the death of an apparently well child twenty minutes after the subcutaneous injection of 1,000 units of antitoxin. The postmortem diagnosis and probable cause of death was status lymphaticus.

Netter³⁰² states that grave accidents following subcutaneous injections of diphtheria serum are rare.

297. Leshke: München, med. Wchnschr., 1915, **62**, 1381.

298. Passler: München. med. Wchnschr., 1916, **63**, 92.

299. Maggiore: *Pediatrics*, 1917, **25**, 193.

300. Sturtevant: *Arch. Int. Med.*, 1916, **17**, 176.

301. Hassler: *California State Med. Jour.*, 1917, **15**, 153.

302. Netter: *Arch. de méd. d enf.*, 1916, **19**, 505.

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THE ETIOLOGY OF PHLYCTENULAR CONJUNCTIVITIS *

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I. CLINICAL OBSERVATIONS

Phlyctenular conjunctivitis is one of the most frequent eye diseases of childhood. Its appearance in typical cases is characteristic. The grayish nodule in or about the cornea, the injection of the surrounding conjunctival vessels, the lacrimation and photophobia present a picture not easily mistaken. The disease is important not only because of the disability which it produces during its active manifestations, but also because the scarring of the cornea which often results in severe or neglected cases produces permanent injury to vision. In spite of numerous investigations into the cause of this conjunctivitis, the etiology has not been definitely determined. Whether the condition is primarily an eye disturbance, or whether it is one of the evidences of constitutional disease, has long been the subject of lively discussion. Moreover, there has been little uniformity of opinion either among those who have contended for its local character or among those who regard it as a manifestation of disease arising outside the eye. Local bacterial infection from without, exposure to wind and dust, errors of refraction, herpes, eczema, pediculosis, diseased tonsils and adenoids, intranasal conditions, gastro-intestinal disturbance, autointoxication, impairment of general health, bad living conditions, scrofula, the exudative diathesis and tuberculosis have at one time or another been put forward as essential or contributing causes of phlyctenular disease.

Among these numerous conflicting views, a few have attracted particular attention. Early writers on the subject observed its frequent occurrence in that peculiar type of constitution known as scrofula. Beer,¹ in 1813, described the condition under the name of conjunctivitis externa scrofulosa. Mackenzie,² in 1833, in an excellent clinical

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1. Beer: *Diseases of the Eye*, 1813, 2, 614; cited by Knorr, E. A., and Maldeis, H. J., *Etiology of Phlyctenular Conjunctivitis*, Maryland Med. Jour., 1913, 56, 90.

2. Mackenzie, William: *A Practical Treatise on the Diseases of the Eye*. From last London edition, Boston, Carter, Hendee & Co., 1833, p. 316.

description of the disease, took a somewhat broader view of the etiology, summarizing his opinion in these words, "Without any hesitation we regard the scrofulous constitution as the chief predisposing cause of this ophthalmia; but we must not omit to mention that other remote causes evidently operate in its production; namely, improper diet, want of air and exercise, and insufficient clothing." Such were the generally accepted views until in the enthusiasm of early bacteriologic research, several investigators claimed that the condition arose as the result of local bacterial infection from without. Later researches, however, did not sustain these findings, and during recent years ophthalmologists have become increasingly convinced that systemic causes are the chief factors in the production of phlyctenular disease.

For several years these cases coming to the eye dispensary of the Northwestern University Medical School have been referred by Dr. Brown Pusey to the children's department with the somewhat embarrassing suggestion that the permanent cure of the eye condition depended on proper constitutional treatment. The fact that the usual routine examination failed to reveal any constant systemic disturbance toward which treatment could be directed suggested the present investigation. Moreover, a review of the literature brought out the interesting fact that practically all investigations into the cause of this condition, admittedly a pediatric problem, have been undertaken by ophthalmologists. The study was carried out under the direct supervision of Dr. Joseph Brennemann of the pediatric staff, to whom I am indebted not only for the general plan of the investigation, but also for sympathetic cooperation in every phase of the work.

The series includes ninety-two cases of phlyctenular conjunctivitis, the diagnosis in every case being made by Dr. Pusey. The clinical study included an exhaustive history, painstaking physical examination, and various laboratory tests, with special attention to the numerous views which have been brought forward concerning the cause of this condition. Among these views the following were considered sufficiently important to merit separate discussion: (1) impairment of general health from whatever cause; (2) bad living conditions; (3) gastro-intestinal disturbance; (4) the exudative diathesis; (5) tuberculosis.

IMPAIRMENT OF GENERAL HEALTH

There has been a widespread belief among writers on phlyctenular ophthalmia, based apparently on general impressions rather than accurate data, that the disease attacks especially the less sturdy individuals, or those whose resistance has been temporarily lowered by improper living or previous illness. In securing the history of each case the mother or other attendant was asked whether the patient was

robust, moderately healthy, or delicate. Sixty-four were considered robust, 16 fairly strong, 12 delicate. On physical examination, 52 were found to be well developed and nourished, 28 with fair physique, 12 decidedly below par. Of the 52 who were well developed and nourished, 17 were noted as being unusually good physical specimens. Their bodies were plump, their flesh firm, their color good; in fact, they were much more sturdy than the average healthy child of the same age.

A special effort was made to ascertain whether the patient or his parents associated the eye condition with any constitutional disturbance. When asked what caused the eyes to become sore, the great majority had no idea whatever. Several thought the trouble was brought on by a cold, though on narrower questioning it was frequently found that the nasal discharge which was the usual evidence of the presence of a cold began after the eye became involved, and was, in fact, caused by the profuse tearing of the affected eye. A few stated that measles brought on the attack, while injury, foreign body, sty, fright, bad blood and run-down condition were given in isolated cases. It is significant that those who had had repeated attacks were unable to associate them with systemic disturbance of any kind. That the illness was usually regarded as local in character and trivial in nature was shown by the attitude towards our work. It was not always easy to convince the mother that the child's illness was sufficiently serious to justify an exhaustive history, complete physical examination and laboratory tests.

It was our purpose to determine whether some distinct physical type, or peculiarity of constitution, or a certain train of circumstances preceding an attack could be established in connection with the eye condition; whether, indeed, it might be possible to say in advance that a given child was a candidate for phlyctenular disease. This we were wholly unable to do. Our cases in general health and development and in the history of previous illness seemed to differ in no particular from patients presenting themselves at our clinic for other complaints.

BAD LIVING CONDITIONS

There is scarcely a writer on phlyctenular disease who omits to mention bad living conditions as a contributing cause. To obtain first hand information concerning the patient's home life, I went into the homes of the first 53 patients studied. The location of the flat or house, the number and size of the rooms, the sleeping rooms, ventilation, surroundings as to light, dust, smoke, etc., were carefully noted. On the data obtained I regarded the living conditions good in 23, fair in 12, poor in 18. Living conditions were considered good only when the family occupied a front flat above ground, with fair light, ventilation, cleanliness and sufficient food. I was especially impressed with

the fact that the appearance of the patients as they present themselves at an outpatient clinic furnishes no criterion for judging home conditions. Coming long distances through dust-swept streets, the hair dishevelled, the face tear-stained and dirty, a soiled handkerchief shielding the affected eye from the light, they would seem to show every evidence of a miserable home environment. Yet on visiting the home I was frequently surprised to find the family in comfortable quarters, the house neat and well-kept, with proper attention to the personal hygiene of the patient. Moreover, in addition to the dispensary cases, the series included 1 nurse in training, 1 medical student, 2 stenographers, and 1 child in the private practice of Dr. Brennemann. Our experience would indicate that bad living conditions are a much less important factor in the production of phlyctenular ophthalmia than is generally taught.

GASTRO-INTESTINAL DISTURBANCE

During recent years intestinal autointoxication has been regarded by many writers as the chief factor in the production of the most varied disorders. In 1905 Elschnig³ attempted to show that certain eye diseases such as iritis, scleritis and iridocyclitis are due to this cause. Colombo,⁴ pursuing the same line of thought, endeavored to establish the importance of auto-intoxication in the etiology of phlyctenular conjunctivitis. The method employed to determine the presence and degree of auto-intoxication was the measure of indican in the urine. In his first paper Colombo reported the finding of indican in the urine in 42 of 43 cases. In a later paper he found indican in large amount in 74 of 115 cases, there being only two in which no indican was detected. That the above findings are not peculiar to phlyctenular conjunctivitis numerous later investigations have abundantly shown. Von Hippe,⁵ in studying 416 cases of eye disease, of which 61 were phlyctenular conjunctivitis, found increased indican no more frequently in this condition than in other diseases of the eye. Stuelp,⁶ in studying the urine in more than 1,000 cases, including not

3. Elschnig: Ueber Augenkrankungen durch Autointoxikation, *Klin. Monatsbl. f. Augenh.*, 1905, **43**, 417.

4. Colombo, G. L.: Ueber die Pathogenese der ekzematösen Keratokonjunktivitis (skrofulösen), *Klin. Monatsbl. f. Augenh.*, 1911, **49**, 164. Die Autodarmintoxikation in der Pathogenese der ekzematösen Keratokonjunktivitis. *Ibid.*, 1912, **50**, 610.

5. Von Hippe, E.: Ueber Indicanurie bei Augenkranken, *Arch. f. Ophth.*, 1912, **81**, 105.

6. Stuelp, O.: Ist die sog. gastrointestinale Autointoxikation (Indicanurie) eine häufige Ursache von Augenkrankheiten? *Arch. f. Ophth.*, 1912, **80**, 548.

only the most varied eye diseases, but also chronic constitutional diseases, found increased urinary indican in practically the same percentage in each group. In the course of extensive metabolism experiments conducted by Long,⁷ Herter,⁸ Folin⁹ and others, in which quantitative estimation of indican on twenty-four-hour specimens was made daily over long periods of time, it was found that there was considerable variation in the amount of urinary indican from day to day; that some individuals had regularly a greater amount of indican than others on a similar diet, and that all showed less indican when the protein in the diet was reduced. For the sake of completeness a quantitative estimation of indican by the Folin method was made in 17 of our cases with the result that 5 showed no indican, 5 a trace, 4 a small amount, 3 a large amount. From the foregoing reports it is seen that indicanuria in varying degree occurs indiscriminately in phlyctenular conjunctivitis, in other eye diseases, in constitutional disease, and in individuals enjoying robust health. Not only is indicanuria an uncertain sign of intestinal auto-intoxication, the term auto-intoxication itself lacks accurate definition. That it has been all too frequently employed to explain conditions otherwise obscure is now generally admitted. In the words of Jaddassohn, "Where a definite etiologic conception is wanting, the word auto-intoxication interposes itself with well-nigh unerring certainty."

In the present state of our knowledge, a careful history concerning gastro-intestinal disturbance would appear to be the more reliable method of estimating its importance in the production of the conjunctivitis. Ten of the patients had poor appetite at the onset of the attack, one had vomiting spells preceding the onset of repeated attacks, one associated each recurrence of the eye trouble with indigestion. Seven suffered from chronic constipation. The remainder gave no history of digestive disturbance of any kind. Considering the series as a whole, they seemed peculiarly free from complaint referable to the gastro-intestinal tract.

EXUDATIVE DIATHESIS

The frequent association of phlyctenular conjunctivitis with scrofula has already been mentioned. Since advances in our knowledge of tuberculosis have demonstrated that the enlarged cervical glands char-

7. Long, J. H.: Investigations on the Effects of Foods Containing Copper Compounds on the General Health and Metabolism of Man, Report 97, U. S. Dept. Agric., June 16, 1913, p. 213.

8. Herter, C. A.: Influence of Saccharin on Digestion, Metabolism, Nutrition and General Health, Report 94, U. S. Dept. Agric., Nov. 15, 1911, p. 13.

9. Folin, O.: Effect of Saccharin on the Health, Nutrition and General Metabolism of Man, Report 94, U. S. Dept. Agric., Nov. 15, 1911, p. 233.

acteristic of scrofula are invariably tuberculous, the term scrofula has been little used, and then usually as a synonym for tuberculous cervical adenitis. Yet this use of the term does not do justice to the original conception of scrofula. It was not the enlarged cervical glands alone, but also the pasty appearance of the patient, the heavy features, the thickened eyelids, nose and lips, the facial eczema, and the tendency to respiratory catarrh which gave to scrofula its distinctive features; and it is precisely these features that cannot be satisfactorily explained by the presence of tuberculosis alone. Of the children who suffer from glandular tuberculosis, only a small per cent. show the skin lesions characteristic of scrofula. To explain these characteristic lesions, Czerny¹⁰ advanced the theory that there is a congenital abnormal tendency to irritative processes in the skin, mucous membranes and lymphatic tissues appearing in certain children. To this condition he gave the name "exudative diathesis," and taught that when children who suffer from this diathesis become infected with the tubercle bacillus they then exhibit the symptoms of scrofula. He summarizes the symptoms as follows:

The symptoms manifest themselves on the skin, the mucous membranes and the lymphoid organs. Among the symptoms appearing on the skin are seborrhea, crusta lactea, strophulus and intertrigo; among those on the mucous membranes are geographic tongue, the periodically occurring catarrh of the nasopharynx, pseudocrop, asthma and recurring bronchial catarrh, *phlyctenular conjunctivitis*, balanitis, vulvitis and certain forms of intestinal catarrh. On the part of the lymphoid organs, this diathesis manifests itself through hyperplasia of the tonsils unassociated with infections, hyperplasia of the spleen, or now and then of many lymphoid organs, namely, that condition which by many authors is regarded as a separate clinical picture under the designation status lymphaticus.

Heubner¹¹ also recognized this condition, and laying stress on the glandular involvement, gave to it the name of lymphatism. Under whatever name it be known, the clinical picture in typical cases is familiar to all students of children's diseases. Yet it becomes at once apparent from the number and variety of the symptoms that the existence of the condition in a doubtful case will be a matter of interpretation on the part of the examiner. If a single symptom were adequate for a diagnosis, few children would escape. What number or grouping of symptoms furnishes positive evidence of the presence of the diathesis? Several of our cases were typical illustrations of this condition, and in some of these the presence of clinically tuberculous cervical glands completed the picture of scrofula. A larger number had facial

10. Czerny, A., and Keller, A.: *Des Kindes Ernährung Ernährungsstörungen und Ernährungstherapie*, Leipsic and Vienna, 1913, 2, 352.

11. Heubner, O.: *Lehrbuch der Kinderheilkunde*, Leipsic, 1911, 2, 33.

eczema. Altogether about one third of our cases showed some eczema, seborrhea, "cradle cap," bronchial catarrh, glandular swellings, or other evidence of the exudative diathesis, or gave a history of such symptoms. Nor was it often possible to secure a history of insufficient gain in weight during the first few months of life, followed by abnormal fatness, symptoms emphasized by Czerny as important features of the condition. Thus it is seen that the phlyctenular conjunctivitis itself was in the majority of instances the only evidence of the presence of the diathesis. That the skin and mucous membranes of certain children are peculiarly susceptible to irritative lesions, there can be no doubt. It might be expected that the tissues of the eye would share this sensitiveness, and that in such cases phlyctenular conjunctivitis would be prone to occur. But the absence of all other evidence of undue tendency towards irritative processes in so large a percentage of cases of the eye disease is a strong argument against such a tendency being alone sufficient to explain the occurrence of the conjunctivitis. Even assuming that phlyctenular conjunctivitis were a manifestation of the exudative diathesis, it would amount only to a restatement of the problem, for the cause of the so-called diathesis is altogether obscure.

TUBERCULOSIS

The frequent occurrence of phlyctenular disease not alone in scrofulous children, but also in those who showed other clinical types of tuberculosis, suggested the possibility of the conjunctivitis resting on a tuberculous basis. The investigation of this question was made the easier because of the introduction of the cutaneous tuberculin test, which gave a ready means of ascertaining more nearly the full incidence of tuberculous infection. The findings of a number of observers who have applied this test are as shown in the table.

The statistics in Table 1 were based chiefly on the von Pirquet method of applying the cutaneous test. The von Pirquet test was used in our cases with the result that the reaction was positive in ninety, negative in two.

A reaction was considered positive if the vaccinated area showed redness 5 mm. in diameter with a negative control. There was, however, seldom any question concerning a positive reaction. Distinct induration and elevation, as well as redness, at the site of the vaccination were almost invariably observed. In only thirteen of the positive reactions was the diameter of the reddened area less than 1 cm. Many were particularly violent, the inflamed areas being 3 to 4 cm. in diameter with superimposed papules or vesicles. A few showed lymphangitis extending several centimeters up the arm, and in a few cases scab formation occurred after the reaction had begun to recede. Thus there

TABLE SHOWING RESULTS OF TUBERCULIN TEST BY DIFFERENT AUTHORS IN
PHLYCTENULOSIS

Author	No. of Cases	No. Positive	Pr. Ct. Positive
Ayrenx ¹²	143	128	90
Bednarski ¹³	100	100	100
Belenky-Raskin ¹⁴	100	92	92
Bruns ¹⁵	102	62	61
Bywater ¹⁶	12	12	100
Davis and Vaugan ¹⁷	40	28	70
Derby ¹⁸	43	38	88
Pyfer ¹⁹	49	41	84
Rosenhauch ²⁰	50	48	96
Tivnen ²¹	50	46	92
Weekers ²²	156*	142	91
Weekers	58†	32	55
Total	903	769	Av. 85

* Children. † Adults.

was found a surprising difference between these patients and others of the same age not alone in the frequent occurrence, but also in the violence of the cutaneous tuberculin reaction.²³

It has been frequently stated that a positive von Pirquet is of little significance, because the majority of children give this test. Yet it must be remembered that the scale of infection is a gradually ascending

12. Ayrenx: *Ophthalmie phlycténulaire et terrain tuberculeux*, *Ann. d'Ocult.*, 1910, **143**, 393.

13. Bednarski: *Ueber die Keratoconjunctivitis phlyctenulosa bei Kindern*, *Klin. Monatsbl. f. Augenh.*, 1911, **49**, 521.

14. Belenky-Raskin: *Zur Aetiologie der phlyktänulären Augenentzündung*, *Zeitschr. f. Augenh.*, 1913, **29**, 503.

15. Bruns, H. D.: *Phlyctenular Ophthalmia and Its Etiology*, *Jour. Am. Med. Assn.*, 1912, **59**, 1002.

16. Bywater, H. H.: *A Note on Phlyctenular Disease*, *Ophthalmoscope*, 1910, **8**, 414.

17. Davis, A. E., and Vaugan, H.: *Phlyctenular (Eczematous) Conjunctivitis and Keratitis with Special Reference to Etiology and the Value of Tuberculin as a Diagnostic Agent: Together with the Report of Forty Cases*, *Ophth. Rec.*, 1912, **21**, 476.

18. Derby, G. S.: *The Increasing Importance of Tuberculosis as a Cause of Ocular Disease. The Newer Methods of Diagnosis and the Treatment*, *Arch. Ophth.*, 1908, **37**, 515.

19. Pyfer, H. F.: *Etiology of Phlyctenular Conjunctivitis and Suggested Treatments*, *Pennsylvania Med. Jour.*, **16**, 184.

20. Rosenhauch, E.: *Ueber das Verhältnis phlyktänularer Augenentzündungen zur Tuberkulose*, *Arch. f. Ophth.*, 1910, **76**, 371.

21. Tivnen, R. J.: *Tuberculin as a Diagnostic and Therapeutic Agent in the Treatment of Conjunctivitis Eczematosa*, *Jour. Am. Med. Assn.*, 1911, **57**, 1886.

22. Weekers, L.: *Nouvelle pathogénie des phlyctènes oculaires*, *Bull. de L'Acad. roy de méd. de Belgique*, 1909, **23**, 577.

23. Positive controls should be employed before accepting a negative von Pirquet test. In vaccinating patients with phlyctenular conjunctivitis after the completion of the above series, I was considerably perturbed by three or four consecutive negative reactions. Persons previously giving a positive reaction were then tested with the same tuberculin with negative results. A representative of the company issuing the tuberculin was interviewed and he said that their recent tuberculin had been found to be inactive and was being recalled.

one reaching the high figures so frequently given only in late childhood. The oft-quoted figures of Hamburger and Monti²⁴ reported among 82 children between the tenth and fourteenth years a positive tuberculin reaction in 94 per cent. Von Pirquet²⁵ found 81 per cent. of positive reactions among 193 children of the same age. In 250 children under 6 years, Hamburger and Monti found a positive result in 26 per cent. Von Pirquet in 821 children of the same age obtained a positive reaction in 18 per cent. Numerous American writers have called attention to the fact that the incidence of tuberculosis is greater in European cities than in this country. Veeder and Johnston²⁶ found in 227 children between the ages of 10 and 14 years at the Children's Hospital in St. Louis a positive reaction in 44 per cent. In 735 children under 6 years, the von Pirquet was positive in 24 per cent. Their figures were compiled from all hospital admissions, including clinical tuberculosis. Excluding these cases the percentage of positive reactions under 6 years was only 12.5 per cent. Even though one accept the higher percentages of tuberculous infection found in European clinics, the figures are in striking contrast to those obtaining for phlyctenular patients of the same age. Thirty-four of Belenky-Raskin's patients with phlyctenular conjunctivitis were under 6 years of age, and 85 per cent. of these gave positive reactions. Weekers found 40 positive reactions in 44 children under 5 years. Among our own cases, 40 occurred in the first five years of life, all but one giving a positive tuberculin test.

In spite of the almost constant presence of tuberculous infection in phlyctenular disease, clinical evidence of tuberculosis has been much less frequently found. A history of direct exposure to tuberculosis was obtained in 29 per cent. of our cases. On physical examination, nine patients showed clinically tuberculous cervical glands or scars from operation, seven had papulonecrotic tuberculids, seven had suggestive findings in the lungs, two had Potts' disease. A distinct D'Espine sign was found in six cases, and in a considerably larger number of cases the findings were suggestive. The total number showing definite clinical signs of tuberculosis equaled 26 per cent.

The presence of tuberculosis in the absence of any other ascertainable cause, either local or general, would suggest that the conjunctivitis rests on a tuberculous basis. Additional facts brought out by Weekers²² and others strengthen this view.

1. The subcutaneous tuberculin test carried out during an attack of phlyctenular conjunctivitis causes an aggravation of the eye symptoms.

24. Hamburger, F., and Monti, R.: Die Tuberkulosehäufigkeit im Kindesalter, München. med. Wchnschr., 1909, **56**, 449.

25. Von Pirquet, C.: Frequency of Tuberculosis in Childhood, Jour. Am. Med. Assn., 1909, **52**, 675.

26. Veeder, B. S., and Johnston, M. R.: The Frequency of Infection with the Tubercle Bacillus in Childhood, AM. JOUR. DIS. CHILD., 1915, **9**, 478.

Weekers found in 10 patients so treated that the eye lesions became distinctly worse in eight.

2. Phlyctenules have occasionally occurred following the diagnostic or therapeutic use of tuberculin subcutaneously.

3. Numerous cases of phlyctenular conjunctivitis have occurred coincidentally with or following a positive ophthalmo-reaction. Such cases have been observed by Wiens and Gunther, Fehr, Bonnetiere and Kleinberger, Feer, Gaupp, Citron, Schenck and Seiffert, Krokiewicz, Kraemer, Fertl, Eppenstein, Schruppf, Freund, Stargardt,²⁷ and Hamman and Wolman.²⁸

4. Weekers performed the ophthalmo-reaction test in five patients who had a history of repeated attacks of phlyctenular conjunctivitis with scars of former lesions, but in none of whom had there been an active process within a year. All of the patients gave a positive reaction, and in three the phlyctenules recurred.

5. Weekers²⁹ and Stargardt²⁷ have studied histologically phlyctenules which occurred as a complication of the Calmette reaction, and found that they correspond to those which occur spontaneously.

Assuming that tuberculosis is the essential cause of the conjunctivitis, the immediate secondary causes which provoke an attack are still to be considered. Absorption from tonsillar infection, intranasal conditions, disorders of the teeth or gums and local irritation from without have been thought to have some relation to the attacks. A careful examination of the nose, throat, ears and sinuses was made by Dr. Carl F. Bookwalter, assistant attending otologist, with the result that the presence of adenoids, diseased tonsils, or nasal deformities was not noticeably greater than among other children of the same age. A large percentage had decayed teeth, but here again the number was not greater than among other dispensary children. Nothing in the history of the patient preceding an attack, nor evidence of local or general disturbance on physical examination, could be found with sufficient uniformity even to suggest its being of importance in provoking the conjunctivitis. In one patient who had been under observation in the hospital for a number of weeks with tuberculous glands of the neck, an attack of phlyctenular conjunctivitis occurred when she was in excellent condition, receiving an abundance of good food, gaining rapidly in weight and the glands showing decided improvement. The physical examination was otherwise negative. The absence of demonstrable

27. Preceding authors cited by Stutgardt, K.: Ueber die Wirkung der Einträufelung von Tuberkulin in den Bindehautsack, *Ztschr. f. Augenh.*, 1909, **22**, 1.

28. Hamman, L., and Wolman, S.: Tuberculin in Diagnosis and Treatment, New York, D. Appleton & Co., 1912, p. 209.

29. Weekers, L.: Anatomie pathologique des phlyctènes oculaires, *Bull. de L'Acad. roy. de méd. de Belgique*, 1910, **24**, 455.

accompanying conditions together with the fact that phlyctenules frequently occur in tuberculous individuals following the use of tuberculin in the eye or subcutaneously would suggest that the condition arises from a disturbance of the equilibrium established between the invading organisms and the host.

The two cases in the series giving a negative von Pirquet deserve special consideration. The first, N. M., a healthy woman, 35 years of age, had a small localized efflorescence on the limbus corneae with moderate injection of the circumcorneal vessels. There had been no previous attack of eye trouble. There was an eruption on the face which had been present for years, diagnosed by Dr. W. A. Pusey as typical acne rosacea. It has been pointed out by various writers that eye lesions in acne rosacea occasionally occur, which closely resemble or are clinically indistinguishable from phlyctenular conjunctivitis. Fuchs³⁰ says:

The characteristic mark of phlyctenular conjunctivitis lies in the focal character of the affection as well as in its localization upon and immediately about the cornea. Only one other variety of conjunctivitis, the conjunctivitis ex acne, shares this peculiarity with phlyctenular conjunctivitis. This affection bears the greatest resemblance to the simple typical picture of phlyctenular conjunctivitis. It is possible to make the differential diagnosis chiefly from the fact that conjunctivitis ex acne attacks only adults and those who are at the same time affected with acne rosacea.

The second case, M. H., a girl 21 months old, had a large, distinct, whitish, sharply circumscribed, elevated area on the ocular conjunctiva of the left eye about 2 mm. from the limbus. The surrounding injection occurred chiefly in the larger rather than the finer vessels of the conjunctiva. Dr Pusey stated that although clinically he thought it should be called phlyctenular disease, it was quite different in appearance from those usually seen. It is also significant that there was not the slightest photophobia or lacrimation, symptoms which are usually severe in children of this age. When the patient returned two days later only a trace of the lesion remained, together with slight injection of the surrounding vessels.

The findings in these two cases suggest the possibility that the lesions were altogether different in kind from those ordinarily found in phlyctenular conjunctivitis. *It is an interesting fact that in no case in which there was a typical efflorescence with characteristic focal injection of the surrounding conjunctival vessels, together with lacrimation and photophobia, was there a negative von Pirquet reaction.*

Finally, the tuberculous theory of the etiology of phlyctenular conjunctivitis brings into harmony the other apparently conflicting opinions of its cause. Impairment of the general health, bad living conditions,

30. Fuchs, E.: Textbook of Ophthalmology (Duane), Philadelphia, J. B. Lippincott & Co., 1911, p. 185.

insufficient food, furnish a favorable opportunity for tuberculosis to gain a foothold. Gastro-intestinal disturbance may be a symptom of obscure tuberculous infection. The exudative diathesis gives a soil favorable to the entrance and growth of the tubercle bacillus which may then produce the clinical picture known as scrofula. These various conditions are seen to be significant inasmuch as they predispose to, or go hand in hand with, tuberculous disease. Their consideration as causative factors strengthens rather than weakens the case for tuberculosis as the one underlying cause of the conjunctivitis.

The foregoing discussion has touched only on the more important features of the clinical study. To make clear the character and scope of the work, and to record data which may be of interest, the outline followed in each case, together with a summary of the findings, is given following:

HISTORY

Age:		Parentage:	
Under 2 years.....	16	Austrian	6
2 to 5 years.....	24	German	5
6 to 10 years.....	24	Irish	4
11 to 14 years.....	7	Bohemian	3
Over 14 years.....	21	Croatian	2
Sex:		Lithuanian	2
Male	30	Scotch-Irish	2
Female	62	Russian	2
Parentage:		German-Irish	1
American	27	Spanish-Bohemian	1
Colored	15	Assyrian	1
Polish	12	Belgian	1
Italian	6	Unknown	2

I. Present Illness.—

1. Present acute attack.

a. Patient's or parent's opinion as to cause:

Unknown	59	Eczema	2
Cold	11	Diphtheria	1
Measles	8	Indigestion	1
Injury	3	Fright	1
Styes	2	Run-down condition	1

b. Symptoms:

1. Local

a. Smarting	10	e. Photophobia	85
b. Burning	11	f. Redness	92
c. Aching	5	g. Lacrimation	87
d. Itching	28	h. Blepharospasm	11

2. General

a. Malaise	10	d. Indigestion	1
b. Headache	2	e. Diarrhea	1
c. Appetite poor in.....	2	f. Fever	0

3. Previous attacks:

a. Occurred in		Worse in summer.....	7
Worse in winter.....	3	Worse in spring.....	1

b. Accompanying conditions in all attacks:

Colds	5	Eczema	2
Blepharitis	2	Indigestion	1
		Run-down condition	1
		Nasal obstruction	1

II. Previous History.—

1. General health:

a. Robust	64
Medium	16
Delicate	12
b. Subject to colds	39

c. Appetite:

Good	81
Fair	5
Poor	2
Variable	4

2. Is patient different from brothers and sisters in physique, activity, mentality or in susceptibility to colds or other catching disease? (No difference in any of these respects noted with sufficient frequency to be of significance.)

3. Tonsils and adenoids

Removed	11
Tonsillitis	7

Mouth breather 6

4. Running ears 8

5. Eczema 24

6. Acute infections:

a. Measles	62
b. Whooping cough	39
c. Scarlet fever	12
d. Diphtheria	16

e. Chicken pox 21

f. Mumps 10

g. Pneumonia 6

7. Tuberculosis:

a. Direct exposure	27
b. Tuberculous glands	12
c. Chronic cough	0

d. Dactylitis 0

e. Tuberculous joint disease. 3

8. Gastro-intestinal tract:

a. Habitual constipation	7
b. Indigestion	3

c. Acute upsets 2

III. Family History.—

1. Father:

Well	72
Tuberculous	4
Dead (3 of tuberculosis)	13
Unknown	3

Tuberculous 3

Dead (3 of tuberculosis) 11

Unknown 1

2. Mother:

Well	77
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3. Brothers and sisters:

Similar eye trouble..... 6

Tuberculosis 10

IV. Hygiene and Environment.—

1. How long in Chicago? How long in present home?

2. If previously in different part of country or in foreign land, was trouble present there?

3. Number in family, including boarders?

4. How much time does patient spend out of doors?

5. If adult, details as to kind of work and sanitary conditions.

6. Food:

a. Amounts of vegetables, meats, eggs, milk and sweets.

b. Use of coffee, tea and alcoholics.

c. Regularity of meals and eating between meals.

d. Usual daily menu.

7. Inspection of home (53 cases):

a. House or flat, front or rear.

b. Number of rooms, size of each.

c. Surroundings as to dust, smoke, etc.

d. Rooms dark or light.

e. Ventilation.

1. How many in sleeping room with patient?

2. Window open in summer? In winter?

3. Method of heating.

From the foregoing data, living conditions considered:		
Good	23	Poor 18
Fair	12	

PHYSICAL EXAMINATION

(Made in every case by Dr. Brennemann)

I. General considerations.—

1. Height, weight, pulse, temperature, respiration.		
2. General appearance.		
Robust	52	Delicate 12
Moderately strong	28	
3. Evidence of scrofula.....	9	Evidence of exudative diathesis 17
Evidence of lymphatism.....	6	

II. Regional examination.—

1. Head:		5. Spine:	
a. Eczema	25	a. Pott's disease	2
b. Seborrhea	14	6. Genitalia and Gluteal Region:	
c. Cradle cap	9	a. Epididymitis, orchitis.....	0
d. Pediculosis	10	7. Extremities:	
e. Thickened nose and upper lip	9	a. Tuberculous hip	1
f. Excoriation about nostrils.	31	b. Dactylitis	0
g. Mouth breather	2	8. Glandular system:	
h. Geographical tongue	6	a. General adenopathy	6
i. Coated tongue	6	9. Skin:	
j. Decayed teeth	44	a. Eczema	25
k. Pyorrhea	11	b. Tuberculids	7
2. Neck:		10. Special report on eyes:	
a. Glands		a. Eye affected	
1. Palpable	59	Left	34
2. Clinically tuberculous..	8	Right	29
3. Chest:		Both	29
a. Heart		b. Number of lesions	
Valvular disease	2	Single	51
b. Lungs		Multiple	41
1. Suggestive of pulmonary tuberculosis	7	c. Location of lesions	
2. D'Espine sign	6	Cornea	41
4. Abdomen:		Limbus	42
a. Enlarged spleen	3	Conjunctiva	5
		Cornea and limbus.....	2
		Conjunctiva and limbus...	2
11. Special report on nose, throat, ears and sinuses (by Dr. Carl F. Bookwalter):			
a. Pathologic tonsils	16	c. Otitis media	4
b. Adenoids		d. Nose	
Small mass	15	1. Rhinitis	10
Moderate mass	13	2. Swollen septum.....	2
Large mass	5	3. Deflected septum	3

III. Laboratory examination.—

1. Von Pirquet test:		Strongly positive	65
Weakly positive (reddened area between 5 and 10 mm.)	13	Violent reaction	12
		Negative	2
2. Complete blood count (made in first 40 cases):			
No characteristic findings. Two showed eosinophilia. Three a mild secondary anemia. All others within normal limits.			
3. Urine examination:			
a. Quantitative estimation of indican (17 cases).			
None	5	Small	4
Trace	5	Large amount	3

B. EXPERIMENTAL OBSERVATIONS

Although the evidence furnished by clinical study seems conclusive enough, the final proof of the nature of phlyctenular conjunctivitis cannot be established in this way. For by this means alone it is impossible to determine whether one is dealing with an etiologic or pathologic entity, or whether the clinical picture represents merely the way in which the tissues of the eye react to various kinds of irritation. The determination of these points rests on bacteriologic, pathologic, and experimental observations.

The localized character of the conjunctivitis at once suggests the possibility of its being produced by a circumscribed infection from without. In the earlier bacteriologic studies of the eye secretions and of the surface of the phlyctenule, several observers found bacteria which they considered to be of more or less importance in producing the condition. Burchard and von Bach,³¹ and Smith³² stated definitely that the lesion was produced by pyogenic cocci, especially staphylococci. Later investigations by von Bach,³¹ Müller,³¹ Neumann,³¹ Axenfeld³¹ and others have shown that the above conclusions were unwarranted. While it is true that the number of organisms in the eye may be increased during an attack of phlyctenular conjunctivitis, this by no means proves that their increase is even remotely concerned in its production. The phlyctenule usually ulcerates, and in such cases, organisms found on the surface of the lesion may well be secondary invaders. As pointed out by Axenfeld,³¹ it would be necessary to demonstrate in the contents of very early phlyctenules the regular presence of a definite number of a given kind of organism before this organism could be assumed to be the cause of the disease. Yet he found that in early cases organisms were often absent, and when found were too few in number and too varied in their nature to draw definite conclusions from their presence. Moreover, numerous attempts to produce phlyctenules in healthy animals by the introduction of various organisms into the eye have proved uniformly negative. In the present state of our knowledge, bacteria from without cannot be excluded as a possible cause of the conjunctivitis; proof that they are of importance is altogether wanting.

The microscopic anatomy of the phlyctenule was first studied by Iwanoff³² in 1869. He showed that the lesion was not a vesicle, as was formerly thought, and as the name phlyctenule itself suggests, but that it consisted of a solid collection of cells. Isolated cases were also

31. Cited by Axenfeld, T.: *The Bacteriology of the Eye* (MacNab), London, Baillière, Tindall & Cox, 1906, p. 253.

32. Iwanoff, A.: *Ueber Conjunctivitis und Keratitis phlyctaenularis*, *Klin. Monatsbl. f. Augenh.*, 1869, 7, 462.

studied by Bass, Gruber, Hertel, Wagemann, Wintersteiner, von Michael, Fuchs, and Leber.³³ Their findings showed considerable variation, due probably in part to the unfavorable conditions under which their material was obtained. The disease is not fatal, it does not require enucleation of the eye, and excision of the phlyctenule as a therapeutic measure has not been seriously advocated. On this account the foregoing studies were restricted almost wholly to cases in which the eye was removed because of some complicating condition, or in which the patient came to necropsy from intercurrent disease. More recently Hayashi and Weekers resorted to the somewhat heroic expedient of excising phlyctenules for microscopic examination, and it is chiefly on their researches that our knowledge of the minute anatomy of the lesion depends.

Hayashi³³ studied five corneal and six conjunctival phlyctenules. In those occurring on the cornea he found the lesion to consist of a collection of leukocytes lying just beneath Bowman's membrane. In early cases the Bowman's membrane and overlying epithelium remained intact. Where the process had progressed farther degeneration and necrosis of the epithelium occurred. In still more advanced cases the more resistant Bowman's membrane had also broken down.

In the conjunctival phlyctenules the cell-collection lay just beneath the epithelium, and in addition to leukocytes, a number of lymphocytes were seen in the lesion, also occasional mast cells and eosinophils. Among the leukocytes larger epithelial cell elements with large pale nucleus and one or several nucleoli were seen. Many of the blood vessels in and about the phlyctenule were distended with blood. Special staining demonstrated the presence of elastic fibers. The epithelium was found to participate in the inflammation. It was irregular, being thinned in places, and in other places thickened and extending into the depth. Its cells were degenerated and not sharply outlined from the underlying tissues. In later cases necrosis and loss of substance occurred.

Weekers²⁹ admirable paper reports the histologic findings in twenty-five cases of phlyctenular conjunctivitis. His series included not only cases occurring in typically scrofulous children, but also three in adults in whom tuberculosis was clinically demonstrable, two in children in whom there was a typical Morax-Axenfeld conjunctivitis at the time of the occurrence of the efflorescence, three arising as complications of the Calmette ophthalmo-reaction. In all of these cases the histology was found to be essentially the same. He says in part:

33. Authors named cited by Hayashi, M.: *Beitrage zur pathologischen Anatomie der Phlyktäne und phlyktäneähnlicher Prozesse*, Klin. Monatsbl. f. Augenh., 1909, 47, 557.

The infiltration consists of leukocytes and epithelioid cells. At first the leukocytes are nearly all polynuclear, mononuclears being rare. In the latter period the mononuclears attain the majority. One sees also sometimes in great number and among the leukocytes epithelioid cells having a large pale nucleus. It is not rare to find among the cells of infiltration, most often beneath the epithelium, multinuclear cells, but the number of the nuclei is never large. They are not the real giant cells of the Langhans type, with numerous nuclei disposed *en collerette*. On the other hand, one observes occasionally in the lumen of the altered vessels giant cells with a single protoplasmic mass and numerous nuclei. Special staining showed the presence of mast cells and eosinophils. The cells of the conjunctival tissue take part in the cellular infiltration, as is shown by numerous mitoses. Although the lymphatic capillaries are dilated, the blood capillaries show hypertrophy of their endothelial cells. Their nuclei are large. The cells project markedly into the lumen of the capillaries. The endothelial cells proliferate. Mitosis is seen. It is not rare to see the endothelial cells disposed in several layers even occlude the lumen of the vessel. The outer margin of the capillaries is less changed, and around their circumference are masses of leukocytes and epithelioid cells.

From the beginning of the efflorescence the epithelium participates in the inflammation. The boundary between the epithelium and subjacent connective tissue is not distinct. In the stage of infiltration the epithelium is thickened. The epithelial cells proliferate, as is shown by karyokinesis. The number of layers is increased. Between the epithelial cells are seen many polymorphonuclear cells and lymphocytes. On the deep surface the epithelium sends prolongations into the underlying tissues. One sees in places degeneration of the epithelial cells. In phlyctenules sufficiently old, there is seen one or more excoriations of the epithelium laying bare the subjacent nodule of infiltration.

In addition to the cases cited, Weekers examined two phlyctenules in adults in whom there was no suggestion of clinical tuberculosis, but in whom there was a history of recent syphilis. Histologic examination showed that the changes were particularly noticeable in the epithelium. It was markedly and irregularly thickened. The infiltration of the subepithelial conjunctival tissue was very moderate and composed chiefly of round cells. He believes that the histology of the lesion is sufficiently different from the cases previously examined to suggest that they may be due to a different cause, and raises the question whether they may be a manifestation of syphilis. Yet his description in these cases is so brief that the exact nature of the difference of cell structure is not altogether clear. Moreover, one of the patients gave a positive cutaneous tuberculin reaction. He does not say whether the test was made in the other case.

The uniformity of the lesions in a rather large series of cases, especially since the series included phlyctenules arising under a variety of conditions, namely, in scrofulous children, in tuberculous adults, in children suffering from Morax-Axenfeld conjunctivitis, and in cases arising from the ophthalmic tuberculin test, would suggest that they were due to a common cause. The lesions were not typical tubercle. No tubercle bacilli, true giant cells, or caseation, were observed. Yet their close relation to certain types of tuberculid led Weekers to the conclusion that they are a similar manifestation of tuberculosis.

The conclusions reached by clinical and pathologic study have been strengthened by animal experimentation.

Bruns³⁴ attempted to produce phlyctenules in rabbits by injecting killed tubercle bacilli into the carotid artery. Thirty-three animals were used. In twelve cases the bacilli were combined with grits of wheat, in five cases with graphite, to increase the probability of organisms finding lodgment in the smaller vessels of the eye. In sixteen cases the bacilli alone were injected. By each of these methods, lesions were produced which resembled phlyctenules clinically, there being all told five successful experiments. Yet Bruns himself admitted that microscopic examination showed important differences between the experimental lesions and human phlyctenules. The lesions did not ulcerate, as usually occurs in phlyctenular disease, and they were found to be distributed throughout the deeper tissues of the eye rather than lying immediately beneath the conjunctival epithelium. Moreover, the microscopic changes showed round cells, epithelioid cells, giant cells, and in some cases clumps of tubercle bacilli. In other words the picture was that of true tubercle. The method employed differed so widely from conditions which obtain in human phlyctenular disease that the experiments would seem to offer little aid in the solution of the problem.

Rosenhauch²⁰ believed that phlyctenular disease occurred in tuberculous individuals when organisms from without produced localized inflammation in the eye. His experiments were directed toward establishing this hypothesis. He found that when he introduced yellow staphylococci into the eyes of healthy rabbits, no phlyctenules occurred. But when the staphylococci were introduced into the eyes of tuberculous animals, phlyctenules occurred almost as a rule. Inasmuch as no organisms of any kind were found in the phlyctenules, he thought that he might be able to use the toxins from the organisms with the same result. For this purpose he injected twenty healthy animals with tuberculin. Into the eyes of ten he introduced killed staphylococci, into the eyes of the other ten he introduced a filtrate from the organisms. In each of the two experiments, phlyctenules occurred seven times. From his experiments he concludes that phlyctenules arise as the result of the combined action of tuberculous toxins, and that of the toxins of external organisms, especially *staphylococcus aureus*.

I regret very much that the war made it impossible to secure Weekers' paper in which his experimental results were given. A summary of his findings as reported by Rubert is as follows: His experiments were carried out on tuberculous rabbits. Pure old tuberculin was instilled into the conjunctival sac four to eight times daily. After

34. Bruns, O.: Ueber experimentelle Erzeugung phlyktäneartiger Entzündungen durch abgetötete Tuberkelbacillen, *Arch. f. Ophth.*, 1904, **58**, 439.

one to three days the conjunctiva became inflamed, and in five cases phlyctenules occurred. Histologically, these phlyctenules showed the same structure as those occurring in scrofulous children. Organisms were not found in the tissues. From his experiments he affirms the tuberculotoxic nature of phlyctenules, but speaks against any etiologic significance of staphylococci, as the phlyctenules arose only when tuberculin was employed. He also introduced tuberculin into the eyes of animals previously injected with tuberculin subcutaneously, but did not obtain phlyctenules in this way.

Rubert³⁵ repeated the experiments of Rosenhauch and Weekers, and also tried other methods of producing the lesions.

He introduced pure old tuberculin into the eyes of tuberculous rabbits and guinea-pigs. In this experiment in which ten rabbits and thirteen guinea-pigs were employed, three rabbits and two guinea-pigs showed lesions which clinically resembled human phlyctenules. All of the rabbits showed a marked conjunctivitis; intense redness of the bulbar and palpebral conjunctiva, swelling of the plica semilunaris, chemosis of the bulbar conjunctiva, and profuse secretion. The guinea-pigs showed much less sensitiveness to tuberculin, five showing no conjunctivitis whatever.

The animals surviving this experiment were then similarly instilled with staphylococcus vaccine. The rabbits showed a marked conjunctivitis, and in one rabbit and two guinea-pigs phlyctenules appeared.

In another experiment healthy animals which had been previously injected with tuberculin subcutaneously received staphylococcus vaccine and tuberculin in the eyes as in the foregoing experiment. One rabbit showed a phlyctenule in each eye when staphylococcus vaccine was being instilled into one eye, and tuberculin into the other.

Experiments on anemic, weakened, and healthy animals did not produce phlyctenules when staphylococcus vaccine and tuberculin were introduced into the eye in the same manner as in the work on tuberculous animals.

Five of the phlyctenules were examined microscopically. Three were found to consist of round cells, while two in addition to the round cells contained also epithelioid cells. No giant cells, caseation or organisms of any kind were seen. Blood vessels could be seen within the nodule; no alteration of the vessel walls was observed. The overlying epithelium was thinned, the cells were flatter than normal, and in the upper layers the cell nuclei often stained poorly. Ulceration occurred in one case.

Because of the somewhat contradictory findings of the above authors, and in order to extend the observations in directions suggested

35. Rubert, J.: Ueber die Aetiologie der phlyktänulären Augenentzündung, *Klin. Monatsbl. f. Augenh.*, 1912, **50**, 273.

by the clinical study, it seemed desirable to carry out a series of animal experiments. The work was done in the laboratory of Dr. A. I. Kendall and to him and his associate, Dr. A. A. Day, I am indebted for many helpful suggestions.

The work was begun with rabbits and guinea-pigs, but it was soon found that the rabbits were more satisfactory because of the larger size and greater sensitiveness of the eye, and all of the later experiments were carried out on rabbits alone. The order of the experiments was influenced by the desire to conserve material.

EXPERIMENTS

Experiment 1.—July 1-3, 1915. *The Effect of Massage on the Eyes of Healthy Animals.* Three rabbits (1, 2, 3) and three guinea-pigs (1, 2, 3) received three minutes' continuous massage three times daily for three days.

Results.—No evidence of inflammation. Rabbits showed slight hyperemia of palpebral conjunctiva and plica semilunaris immediately following massage, which disappeared within a few minutes. The guinea-pigs showed occasionally a very slight hyperemia of the palpebral conjunctiva, less noticeable than in the rabbits.

Experiment 2.—July 7-9, 1915. *The Effect of the Instillation of Tuberculin Into the Eyes of Healthy Animals.* Twelve rabbits (1-12) and eleven guinea-pigs (1-11) each received 1 drop of pure old tuberculin in the right eye three times daily for three days. Instillations made at 9 a. m., 1 p. m. and 4 p. m. Three minutes' continuous massage followed instillations in half of each group of animals.

Results.—No evidence of conjunctivitis in any case. In the guinea-pigs there was occasional slight hyperemia following massage, though no more than was observed in the first experiment where massage alone was employed. In the rabbits no change was observed when the tuberculin was introduced without massage. When massage was employed, there was regularly a transient hyperemia of the palpebral conjunctiva and plica semilunaris, apparently a little greater than when massage alone was employed. Rabbit 1 was extremely emaciated and appeared very ill during the experiment, yet the eye reacted similarly to those of rabbits in good health.

Experiment 3.—July 26-28, 1915. *The Effect of the Instillation of Staphylococcus Vaccine Into the Eyes of Healthy Animals.* Seven guinea-pigs (2, 3, 4, 6, 8, 10, 11) and eleven rabbits (2-12) each received 1 drop of staphylococcus vaccine in left eye three times daily for three days. Normal salt solution used similarly in right eye as control. Massage was employed in half of the animals. The vaccine was obtained from a culture of *Staphylococcus aureus*, the virulence of which for rabbits was established by the fact that a purulent keratitis resulted when organisms were injected into the cornea. Weight of vaccine, 1 billion per cubic centimeter.

Results.—Guinea-pigs: no conjunctivitis. Occasional slight hyperemia of palpebral conjunctiva following massage, no more noticeable in eye into which vaccine was introduced than in control eye. Pig 8 was very weak and emaciated at beginning of experiment, and died after twenty-four hours. Eyes showed no reaction.

Rabbits: no conjunctivitis. When staphylococcus vaccine was used without massage no change was observed. When massage was employed, there was temporary hyperemia of the palpebral conjunctiva and plica semilunaris but no more marked in the eye into which vaccine was instilled than in the control eye into which normal salt solution was introduced.

Experiment 4.—July 29, 1915. *The Effect of a Second Instillation of Tuberculin Into the Eyes of Healthy Animals.* Three rabbits (2, 6, 10) and three guinea-pigs (2, 4, 10) each received 1 drop of pure old tuberculin at 9 a. m., 1 p. m. No massage. These animals had received tuberculin in the same eye three times daily for three days (July 7-9).

Results.—No reaction in any case.

Experiment 5.—July 30-Aug. 25, 1915. *The effect of the instillation of normal horse serum into the eyes of healthy animals following subcutaneous injection of horse serum; the effect of the injection of normal horse serum subcutaneously following the instillation of horse serum into the eyes.*

Six rabbits (7, 8, 9, 10, 11, 12) and two guinea-pigs (10, 11) were injected subcutaneously with 0.5 c.c. of normal horse serum. Five rabbits (2, 3, 4, 5, 6) and three guinea-pigs (2, 3, 4) received 2 drops of normal horse serum in the right eye.

Twenty-four days later (August 23) Rabbits 2, 3, 4 and 5 and Guinea-pig 4, all of which had received horse serum in the right eye, were injected with 0.5 c.c. of horse serum subcutaneously. The animals which had been injected subcutaneously July 30 received instillations as follows: August 23, Rabbit 7 received one instillation of 3 drops of horse serum. August 24, Rabbit 8 received 3 drops of horse serum in the right eye at 9 a. m., at 1 p. m. and at 4 p. m. August 25, Rabbits 9 and 12 and Guinea-pig 10 received 3 drops of horse serum in the right eye at five-minute intervals for an hour. Rabbits 10 and 11 received 2 drops of horse serum in the right eye at five-minute intervals for two hours.

Results.—No reaction in any case.

Experiment 6.—Aug. 30-Sept. 18, 1915. *The effect of the instillation of tuberculin and of staphylococcus vaccine into the eyes of healthy animals following the injection of tuberculin subcutaneously.*

Nine rabbits (2, 4, 5, 7, 8, 9, 10, 11, 12) and two guinea-pigs (4, 10) received 1 c.c. of 5 per cent. old tuberculin subcutaneously. Twelve healthy rabbits (13-24), not previously used, received 0.2 c.c. of 5 per cent. old tuberculin subcutaneously. Rabbit 11 died September 1. Rabbits 2, 4, 5 and 9 were killed because of "snuffles." None had shown conjunctivitis.

Beginning September 16, seventeen days after the subcutaneous injection of tuberculin, four rabbits (7, 8, 10, 12) and two guinea-pigs (4, 10) received 1 drop of pure old tuberculin in left eye three times daily for three days. Rabbits 7 and 8 and Guinea-pig 4 were given three minutes' continuous massage following each instillation. Beginning September 21 the remainder of the rabbits received tuberculin in the left eye and staphylococcus vaccine in the right eye as follows:

Rabbits 13, 14, 15, three times daily for two days; 13 and 15, three minutes' massage.

Rabbits 22, 23, 24, three instillations daily for one day.

Rabbits 19, 20, 21, hourly instillations one day from 9 a. m. to 5 p. m. Rabbit 20 had three minutes' massage after each instillation.

Rabbits 16 and 17 were instilled every five minutes for two hours.

The staphylococcus vaccine was from a strain of *Staphylococcus aureus hemolyticus*, which produced pyemia when injected into the ear vein of a rabbit. Weight of vaccine, 1 billion per cubic centimeter.

Results.—No conjunctivitis. Slight transient hyperemia in cases in which massage was employed, and in those instilled every five minutes, due apparently in the latter to frequent manipulation. Rabbits 10 and 15 died shortly after completion of the experiment, and though they had been in poor condition for several days, they gave no reaction.

Experiment 7.—Sept. 30-Nov. 12, 1915. *The effect of the instillation of tuberculin into the eyes of tuberculous animals.*

September 30, twelve rabbits (8, 12, 13, 14, 16, 17, 19, 20, 21, 22, 23, 24) and two guinea-pigs (4, 10) received 0.1 mg. of a culture of bovine tubercle bacilli intraperitoneally. Temperatures and weights were taken every second day. Guinea-pig 10 died October 19. Necropsy showed generalized tuberculosis. Inasmuch as Rabbits 12, 13, 14, 17, and 22 and Guinea-pig 4 had shown elevation of temperature for several days, instillation of tuberculin was begun October 20. One drop of pure old tuberculin was introduced into the right eye four times daily (9 a. m., 12 m., 2 p. m., 4 p. m.) for three days, except Rabbits 17 and 22, which received three instillations daily during the same period. Rabbits 12 and 13 and Guinea-pig 4 received three minutes' massage following each instillation.

Results.—Guinea-pig 4 showed hyperemia of the palpebral conjunctiva with increased secretion twenty-four hours after beginning the instillation. It died the following day. The rabbits, without exception, showed conjunctivitis, beginning twenty-four to thirty-six hours after the first instillation of tuberculin. The reaction was limited chiefly to the palpebral conjunctiva and was not severe in any case. Rabbit 13 showed also injection of the vessels of the bulbar conjunctiva in the region between 11 and 1 o'clock. The reactions reached their height on the third day, and all had disappeared on the fifth day. Reactions were not noticeably influenced by massage.

October 27. Four rabbits (12, 19, 20, 24) received 1 drop of pure old tuberculin in left eye four times daily for three days. Two rabbits (13 and 22) received 1 drop of pure old tuberculin hourly from 9 a. m. to 5 p. m. during one day. No massage.

Results.—Rabbit 12 died twenty-four hours after beginning the experiment. Eye gave no reaction. Rabbits 19 and 20 showed moderate hyperemia of palpebral conjunctiva. Rabbits 13, 22 and 24 gave a much more marked reaction. In addition to involvement of palpebral conjunctiva, there was redness of the plica semilunaris and ocular conjunctiva with profuse, stringy secretion. October 28, a small, sharply defined circular grayish-white spot just internal to the limbus was seen in the left eye of Rabbit 13. Dr. Pusey pronounced it a tubercle of the iris. The animal died November 3, and microscopic examination confirmed the diagnosis. On the morning of October 29, Rabbit 22 was unable to open the left eye because of the thick secretion which held the lids together. Examination showed intense injection of the palpebral conjunctiva, with mild injection of the circumcorneal vessels. In the inner lower quadrant about 1 mm. external to the limbus there was a grayish, circumscribed, elevated area, pinhead in size, with hyperemia of surrounding vessels. The lesion resembled phlyctenule clinically. Eye enucleated.

November 3. Two rabbits (8, 16) received 1 drop of pure old tuberculin in right eye four times daily for three days.

Two rabbits (19, 21) received 1 drop old tuberculin in right eye eight times daily for three days.

Two rabbits (23, 24) received 1 drop of pure old tuberculin in right eye every fifteen minutes for two hours.

Results.—Rabbits 8, 16, and 21 showed slight injection of palpebral conjunctiva and plica semilunaris eight hours after the instillations were begun. On the following day all rabbits showed violent reactions; intense redness of palpebral conjunctiva and plica semilunaris, moderate injection of the ocular conjunctiva, with profuse, thick secretion. Rabbits 16 and 23 showed more marked injection of ocular conjunctiva in region between 11 and 1 o'clock. Reactions were at their height on the second and third days and disappeared completely on fifth or sixth days. In these cases the reaction seemed about equally severe despite the variation in time interval and the number of instillations made.

November 9. Six rabbits (8, 16, 19, 21, 23, 24) received 1 drop of old tuberculin in left eye four times daily for three days. No massage. Rabbits 19 and 24 had had tuberculin in left eye October 27-29.

Results.—Rabbit 19 was very feeble and emaciated, and showed no reaction. All others gave marked reaction, similar to that heretofore described. November 10 there was seen in Rabbit 8 an indistinct, grayish-white, circumscribed area at the limbus at 6 o'clock, with injection of surrounding vessels. There was also a distinct localized, grayish, raised area the size of a large pinhead on the limbus at 8 o'clock, with hyperemia of the neighboring conjunctival vessels. On the following morning the nodule at 6 o'clock was less distinct, the lesion at 8 o'clock was still plainly visible. The lesion was diagnosed as phlyctenule by Dr. Pusey. Eye enucleated.

Rabbit 23, which had given a very violent reaction, showed on the morning of November 12, one circumscribed, grayish area at 6:30 o'clock, one at 7 o'clock, three close together at 8 o'clock, all situated at the sclerocorneal junction. The lesions were pinhead in size. There was a diffuse injection of the conjunctival vessels, but this was much more marked immediately surrounding the lesions. Eye enucleated November 12.

Experiment 8.—Nov. 18-24, 1915. *The effect of the instillation of staphylococcus vaccine into the eyes of tuberculous rabbits.*

Four rabbits (16, 19, 21, 24) received 1 drop of staphylococcus vaccine in right eye four times daily for three days, beginning November 18. Three of the rabbits (16, 21, 24) received similar instillations in left eye beginning November 22. Vaccine from same source as that employed in Experiment 3. Weight, 1 billion per cubic centimeter.

Results.—Rabbit 16 showed moderate redness of palpebral conjunctiva and very slight injection of ocular conjunctiva on the morning of the second day of instillation into left eye. This was very transient, disappearing within a few hours. Others gave no reaction. Rabbit 19 died twenty-four hours after beginning of experiment.

November 29. Rabbit 24 was very feeble at the conclusion of the foregoing experiment. Others appeared in good condition. Thinking, however, that the failure to react to staphylococcus vaccine might be explained by the fact that the tuberculosis was progressing rapidly, it was decided to ascertain whether the eyes remained sensitive to tuberculin. Instillations were made four times daily for three days.

Results.—Rabbit 24 showed a very mild conjunctivitis, which began to recede on the second day. Rabbit 21 gave a moderate reaction. Rabbit 16 gave a violent reaction beginning six hours after the first instillation. There was marked redness and edema of the palpebral conjunctiva, with injection of the plica semilunaris and bulbar conjunctiva. December 1, three small grayish nodules, pinhead in size were seen on the limbus in the region between 5 and 6 o'clock, with increased injection of surrounding conjunctival vessels. On the following day two of the lesions were still seen distinctly. Eye enucleated.

Experiment 9.—Nov. 25-Dec. 30, 1915. *The effect of the instillations of tuberculin into the eyes of tuberculous rabbits not previously subjected to experimentation.*

Inasmuch as the eyes of the rabbits used as heretofore described had been instilled repeatedly both before and after they were made tuberculous, it might be claimed that the lesions produced were the result of the cumulative action of the various irritants. To meet this possible objection, also to secure, if possible, a greater number of phlyctenules for study, twelve additional rabbits (25-36) were injected with 0.1 mg. of a bovine culture of tubercle bacilli, Nov. 25, 1915. A few days later Rabbits 25, 32 and 36 were killed because of "snuffles."

December 20. Nine rabbits (26, 27, 28, 29, 30, 31, 33, 34, 35) received 1 drop of pure old tuberculin in right eye four times daily for three days.

Results.—Rabbit 30 gave no reaction. Rabbit 33 showed very mild reaction beginning on the third day. There was redness of the palpebral conjunctiva, with moderately increased secretion. All others gave severe reactions similar to those described above when similar instillations were made. December 22,

Rabbit 31 showed localized injection of the lower quadrants of the conjunctiva, and in the region of 5 o'clock, 1 mm. from the limbus, a grayish, circumscribed area pinhead in size. December 23, the same area was still visible, and near it were seen two other grayish areas with narrow hyperemic band leading to them from a peripheral direction. December 24, the lesion at 5 o'clock could be seen indistinctly, the other two had disappeared. December 25, only slight localized hyperemia remained. On the following day this had disappeared.

December 21, Rabbit 35 showed, in addition to generalized conjunctivitis, a marked injection of the larger conjunctival vessels of the lower quadrants of the ocular conjunctiva, also slight, diffuse injection in this region. December 22, there was seen a distinct grayish nodule on the limbus at 6 o'clock. It was the size of a large pinhead and encroached on the corneal tissue. The lesion had the typical appearance of phlyctenule. Eye enucleated December 23.

December 29. The conjunctivitis from the foregoing experiment having disappeared, the eyes of the rabbits were examined preparatory to instilling staphylococcus vaccine into the left eye. In the left eye of Rabbit 31 were seen three beautiful phlyctenules. One about 1 by 2 mm. in diameter was situated 2 mm. from the limbus at 12:30 o'clock, the size of a pinhead, one of same size at the limbus at 8 o'clock. All were distinctly elevated, sharply circumscribed, with slight injection of finer conjunctival vessels immediately surrounding them. In addition, the first was surrounded by a mesh of larger vessels, the second had a vessel leading to it from the periphery, also a vessel extending from it to the first nodule. A branching vessel lay external to the third lesion. On the following day there was seen on the palpebral conjunctiva of the lower lid about 2 mm. from the fornix and about 3 mm. medial to the midpoint between the canthi, a sharply circumscribed, grayish nodule, surrounded by a narrow zone of fine vessels, with one larger vessel leading toward the inner canthus. The branches of this vessel encircled the nodule. Eye enucleated December 30.

The appearance of the efflorescences in this case was precisely that of the typical human phlyctenule. There was no generalized conjunctivitis. No instillation of any kind had been made into the affected eye. The animal had had tuberculin in the right eye the previous week, at which time a severe reaction occurred with three small lesions resembling phlyctenules.

Experiment 10.—Jan. 3-5, 1916. *The effect of the instillation of staphylococcus vaccine into the eyes of tuberculous rabbits. The eye into which the vaccine was instilled not previously subjected to irritation of any kind.*

Seven rabbits (26, 27, 28, 29, 30, 33, 34) received one drop of staphylococcus vaccine in left eye four times daily for three days. Vaccine was obtained from *Staphylococcus aureus* which had been passed through rabbit, producing multiple abscesses. Weight of vaccine, 3 billion per cubic centimeter.

Results.—January 4, Rabbit 34 showed very slight localized circumcorneal injection in the outer lower quadrant. On the following day there was seen a fairly distinct, very small circumscribed grayish area about 0.5 mm. from the limbus in the inner lower quadrant. The area was about 0.5 mm. in diameter and did not appear to be raised. A slight degree of surrounding hyperemia, chiefly in linear direction, extended from periphery to the lesion. On the following day the eye appeared perfectly normal. Other rabbits gave no reaction.

Experiment 11.—Jan. 26, 1916. *The effect of the subcutaneous injection of tuberculin on the eyes of tuberculous rabbits.*

Six rabbits (27, 28, 29, 30, 33, 34) used. Temperature taken at 10 a. m. At 3 p. m. they received old tuberculin subcutaneously as follows:

	Mg.		Mg.
Rabbit 27.....	0.1	Rabbit 30.....	1.0
Rabbit 28.....	0.2	Rabbit 33.....	5.0
Rabbit 29.....	0.5	Rabbit 34.....	10.0

Results.—Temperatures were taken at 10 a. m., January 27, and January 28. No distinct rise occurred in any case, the variation being no greater than on days previous to the injection. The animals showed no evidence of discomfort, and no eye disturbance was observed.

Experiment 12.—Feb. 4, 1916. *The effect of a single instillation of pure old tuberculin into the eyes of tuberculous rabbits.*

Two rabbits (33, 34) received 2 drops of pure old tuberculin in left eye.

Results.—Rabbit 33 did not react. February 5, Rabbit 34 showed mild hyperemia of the palpebral conjunctiva. There was very slight injection of the vessels in the inner lower quadrant of ocular conjunctiva. The reaction persisted for about twenty-four hours.

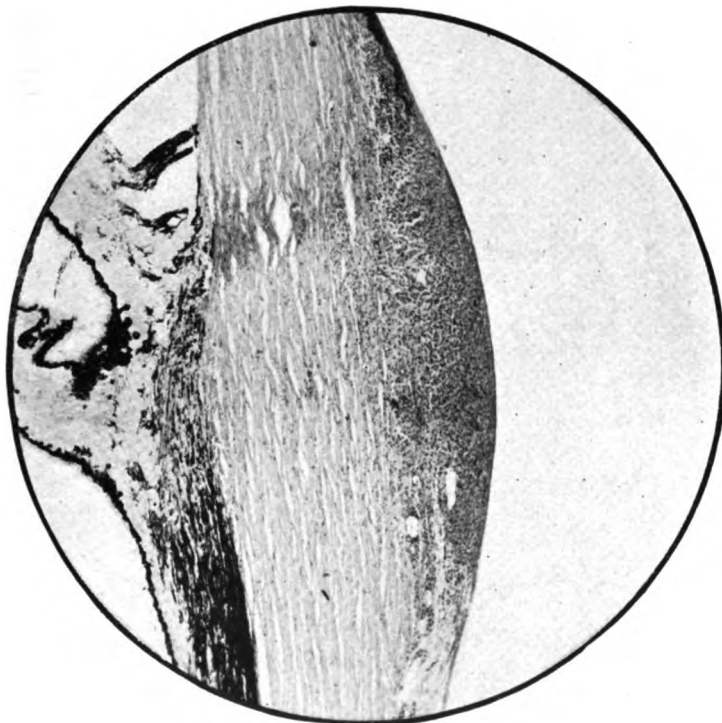


Fig. 1.—Eye 31. Phlyctenule occurring in tuberculous rabbit without instillation of any kind into the affected eye. Photomicrograph $\times 60$.

Experiment 13.—Feb. 4, 1916. *The effect of a single instillation of 1 per cent. old tuberculin into the eyes of tuberculous rabbits (Calmette).*

Three rabbits (27, 28, 29) received 2 drops of 1 per cent. tuberculin in the left eye.

Results.—No reaction.

Experiment 14.—March 10, 1916. *The effect of the injection of tuberculin beneath the conjunctival epithelium of tuberculous rabbits.*

Three rabbits (27, 28, 29) used. With a fine needle 1 drop of 10 per cent. old tuberculin was injected beneath the conjunctival epithelium of the right eye. Injection made about 3 mm. from limbus in upper, outer quadrant.

Results.—After twenty-four hours, hyperemia of the conjunctiva occurred around the point of injection. The reactions were not severe, and persisted only about forty-eight hours. There was no generalized conjunctivitis.

Experiment 15.—Feb. 8-April 20, 1916. *The effect of tuberculosis on the eyes of young rabbits.*

The rabbits previously used were sturdy, full-grown animals. Inasmuch as phlyctenular conjunctivitis occurs much more frequently in children than in adults, it was thought that phlyctenules might be produced more readily in growing animals. Twelve half-grown rabbits (37-48) were injected intraperitoneally with 0.05 mg. of a bovine culture of tubercle bacilli on Feb. 8, 1916.

Five of the rabbits (37, 38, 40, 43, 44) were not subjected to further experimentation, but were kept under daily observation until they succumbed to their tuberculous infection.

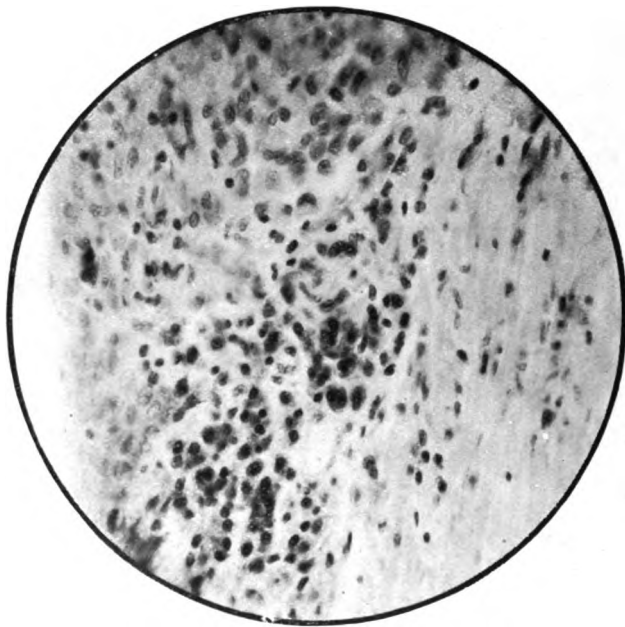


Fig. 2.—Eye 31. High power photomicrograph from section shown in Figure 1. $\times 350$.

Results.—No phlyctenules or other eye disturbances observed.

Experiment 16.—March 9, 1916. *The effect of the subcutaneous injection of very large doses of tuberculin on the eyes of tuberculous young rabbits.*

Four rabbits (45, 46, 47, 48) used. They had shown distinct elevation of temperature for several days. Temperatures taken at 10 a. m. March 9. At 3 p. m. they received pure old tuberculin subcutaneously as follows:

Mg.	Mg.
Rabbit 45..... 1	Rabbit 47.....100
Rabbit 46.....10	Rabbit 48..... 1 (gm.)

Results.—No eye disturbance observed. Rabbit 46 was in very poor condition at time of injection and died two days later. Other animals showed no evidence of discomfort. Temperatures were taken at 10 a. m. March 10 and 11. No distinct rise occurred, the variations being no greater than on days previous to the injection.

The three surviving animals were not submitted to further experimentation. April 6, there was seen in the left eye of Rabbit 48 a localized hyperemic area adjacent to the limbus at 8 o'clock. At the corneal margin in the midst of the injected region was a grayish circumscribed area the size of a small pinhead, not definitely elevated. On the following day the injection of the conjunctival vessels was less marked, but the nodule was more distinct. Dr. Pusey declared that it was probably a phlyctenule. In addition to the lesion mentioned, there was a small hyperemic area adjacent to the limbus at 2 o'clock. There was no generalized conjunctivitis. Eye enucleated April 7.

April 12, there was seen in the left eye of Rabbit 45 an elevated, circumscribed vesicular lesion, pinhead in size. It was located at the limbus at

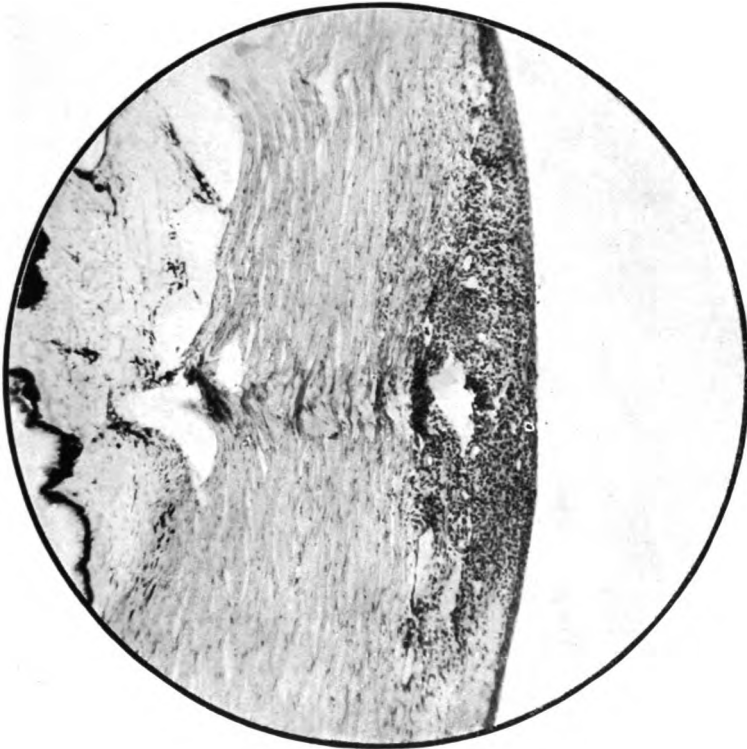


Fig. 3.—Eye 48. Phlyctenule occurring in tuberculous rabbit without instillation of any kind into either eye. Photomicrograph $\times 90$.

12 o'clock. The surrounding conjunctival vessels were injected. A diagnosis of herpes conjunctivae was made by Dr. Pusey.

Experiment 17.—April 4, 1916. *The effect of the injection of pure old tuberculin beneath the conjunctival epithelium of tuberculous young rabbits.*

Three rabbits (39, 41, 42) used. With a fine needle 1 drop of pure old tuberculin was injected beneath the conjunctival epithelium of the left eye in the upper outer quadrant.

Results.—Rabbit 39 was in very poor condition and died at the time of injection. After twenty-four hours Rabbits 41 and 42 showed hyperemia of the conjunctival vessels surrounding the point of injection. This hyperemia extended from the corneal margin to the fornix, and in Rabbit 42 there was

also hyperemia of the upper lid conjunctiva. The reaction was at its height on the second day, then gradually disappeared. The rabbits were kept under observation until death without further noticeable eye disturbance.

Necropsy was performed on all animals used in the foregoing experiments. Generalized tuberculosis was found in all cases inoculated with tubercle bacilli, except in a few that died of intercurrent infection before sufficient time had elapsed for tuberculosis to develop. It was not found in any animal which had not been injected with tubercle bacilli.

DISCUSSION

It will be seen from the foregoing experiments that in eight instances lesions occurred which clinically resembled phlyctenules. They were situated at the limbus or in the adjacent conjunctival tissue, and were about pinhead in size. Injection of the surrounding conjunctival vessels was always observed. All occurred in tuberculous rabbits. In six cases the lesions appeared at the height of a more or less severe generalized conjunctival reaction resulting from the instillation of tuberculin. In two cases phlyctenules occurred in the absence of any known local irritation. No instillations had been made into the affected eye, and there was no generalized conjunctivitis. In one (Rabbit 48) the phlyctenule was so indistinct that the clinical diagnosis was made with some reservation. In the other (Rabbit 31) were seen four typical phlyctenules, three on the ocular conjunctiva, and one on the palpebral conjunctiva.

Following the instillation of staphylococcus vaccine into the eyes of tuberculous animals, no reaction was observed save in two instances, when a localized injection of the ocular conjunctiva occurred. The occurrence of the conjunctivitis in only two cases out of many trials, and the fact that similar transient localized inflammations were occasionally observed in control animals, raise the question whether the vaccine produced the reactions. The repeated instillation both of tuberculin and staphylococcus vaccine into the eyes of healthy animals, and animals previously injected with tuberculin, proved altogether negative.

That phlyctenular conjunctivitis may be an anaphylactic reaction has been suggested. Von Szily³⁶ found that a typical anaphylactic reaction occurred in the cornea when horse serum was injected into the cornea of an animal previously sensitized by subcutaneous injection of horse serum. It seemed desirable to ascertain whether a reaction would occur when the serum was merely instilled into the eye instead of being injected into the cornea, and whether, indeed, phlyctenules might be produced in this way. Results of the experiment were uniformly negative.

36. Von Szily, A.: Ueber die Bedeutung der Anaphylaxie in der Augenheilkunde, *Klin. Monatsbl. f. Augenh.*, 1913, **51**, 164.

The foregoing findings differ in several particulars from those of Rosenhauch and Rubert. Rosenhauch reported the occurrence of phlyctenules almost as a rule when staphylococci were introduced into the eyes of tuberculous animals, and in the great majority of cases when staphylococcus vaccine was instilled into the eyes of healthy animals previously injected with tuberculin. Yet one reads his paper with a feeling of disappointment. The lesions produced were not described in detail, whether they were accompanied by localized or

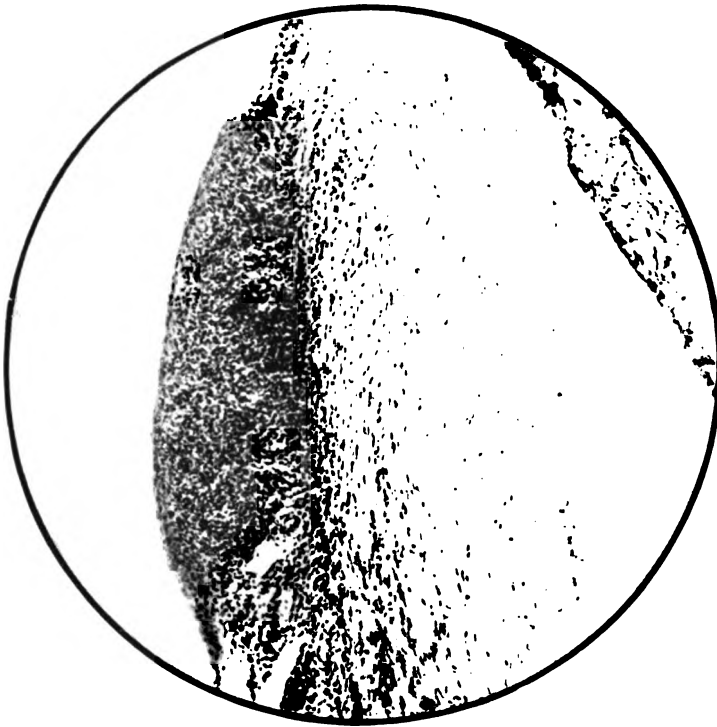


Fig. 4.—Eye 35. Phlyctenule occurring in tuberculous rabbit at the height of a conjunctival reaction resulting from the instillation of tuberculin. Photomicrograph $\times 110$.

generalized conjunctivitis was not stated, and in only two cases were microscopic findings reported. Complete omission of the technic followed made exact repetition of his work impossible. It is regrettable that results so brilliant were so inadequately reported.

Rubert found that instillation of staphylococcus vaccine into the eyes of tuberculous rabbits occasionally produced phlyctenules, and regularly produced a more or less severe diffuse conjunctivitis. Since this did not occur in healthy animals following the instillation of staphylococcus vaccine, he concluded that tuberculosis causes increased

sensitiveness of the eye to various forms of irritation. My experimental studies failed to confirm this conclusion. Save for the specific action of tuberculin, the eyes of tuberculous animals showed no greater sensitiveness than those of healthy animals.

PATHOLOGICAL EXAMINATION

Five eyes showing phlyctenules were studied microscopically. The animals were killed with chloroform, and the eyes enucleated at once. They were fixed in Zenker's fluid, hardened in alcohol, and embedded in paraffin. Sections were stained with hematoxylin and orange G.

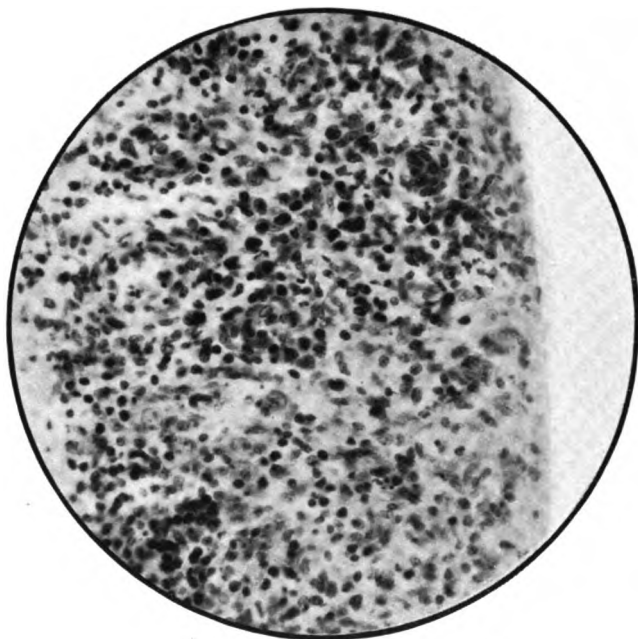


Fig. 5.—High power photomicrograph from section shown in Figure 4. $\times 350$.

Other stains were employed to bring out special features and to examine for organisms. The microscopic anatomy interpreted by Dr. J. P. Simonds is as follows:

EYE 31 (Figs. 1 and 2).—Phlyctenule occurring in tuberculous rabbit without instillation of any kind into the affected eye.

Cell Exudate.—The phlyctenule consists of a circumscribed mass of cells lying directly beneath the epithelium, extending peripherally from the corneal margin. The lesion is composed largely of epithelioid cells. These are large, oval or polygonal cells, larger than polymorphonuclear leukocytes, with oval or irregular eccentric nuclei and abundant nongranular cytoplasm. They are identical in all respects with the type of cell described by Mallory as the endothelial leukocyte. Scattered among these cells are a few polymorphonuclear

leukocytes. Near the periphery of the nodule is a zone of round cells of the lymphocyte type. No giant cells or caseation are seen. In the conjunctival tissue outside the phlyctenule are a few plasma cells. (Unna-Pappenheim stain.) In the cell mass are areas in which an occasional cell has undergone necrosis, the nucleus disintegrating by karyorrhexis. A few fibroblasts are seen. Mitoses are fairly frequent.

The blood vessels at the periphery are surrounded by small round cells.

Epithelium.—At the margins of the phlyctenule the epithelium is irregular. Blunt finger-like processes dip into the subjacent tissue. Over the most prominent part of the phlyctenule the epithelium is very thin; the superficial flatter layers are missing. At one point ulceration has occurred. Polymorphonuclear cells are found among the epithelial cells, most numerous near the point of ulceration.

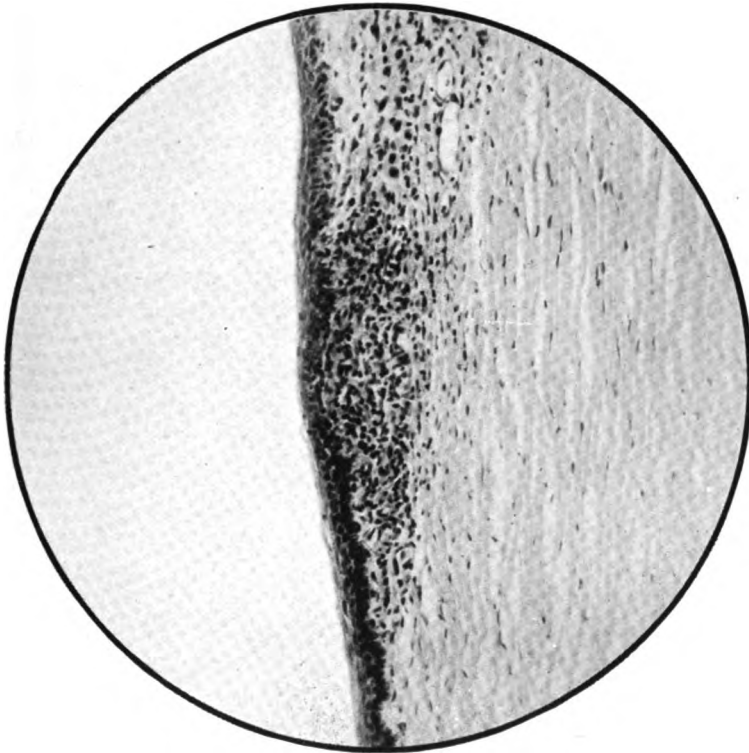


Fig. 6.—Photomicrograph through limbus in Eye 35 at some distance from the phlyctenule. $\times 180$.

The three other phlyctenules occurring in this eye show a structure in all respects similar to that described above, except that in the one on the palpebral conjunctiva there is seen at one point a roughly circular mass of epithelioid cells almost completely surrounded by a zone of small, round, lymphocyte-like cells, thus suggesting in some respects an epithelioid tubercle.

EYE 48 (Fig. 3).—*Phlyctenule occurring in tuberculous rabbit without instillation of any kind into either eye.*

This phlyctenule is smaller than those in Rabbit 31, but its general structure is essentially the same. There are relatively fewer epithelioid cells, and polymorphonuclear cells are somewhat more abundant. Cell necrosis is seen more

frequently. Occasional mitoses are observed. In places the endothelium of the vessels is swollen, but there is no proliferation. The epithelium is irregular at the margins of the phlyctenule, and thinned over the most prominent part, but it appears intact throughout.

Eye 35 (Figs. 4 and 5).—*Phlyctenule occurring in tuberculous rabbit at the height of a conjunctival reaction resulting from the instillation of tuberculin.*

Cell Exudate.—The phlyctenule is situated at the limbus just beneath the conjunctival epithelium. The lesion consists of a mass of closely packed cells. Epithelioid cells are seen, though much less abundant than in the phlyctenules described. These cells are overshadowed by the larger number of small round cells of the lymphocyte type. Among these are many polymorphonuclear leukocytes. Mitoses are frequent. Plasma cells are present in the neighborhood of the lesion, but not in the cell mass itself.

The endothelium of the capillaries has proliferated. Some of the vessels are partially, others totally occluded by this proliferation, so that the original site of many vessels is indicated by an "endothelial whorl." Polymorphonuclear leukocytes in considerable numbers are seen surrounding the vessels at the periphery of the lesion.

Epithelium.—The epithelium at the margins of the phlyctenule is irregular. Over the summit it is thinner than normal; the superficial flatter layers are missing, but at no point is there a break in continuity. There are present a considerable number of cells filled with mucus, with the nucleus flattened against the base of the cell. Among the epithelial cells are many polymorphonuclear leukocytes.

Eye 16.—*Phlyctenule occurring in tuberculous rabbit at the height of a conjunctival reaction resulting from the instillation of tuberculin.*

Findings are essentially the same as in Eye 35. The changes in the blood vessels are less marked. Epithelioid cells are more abundant toward the periphery, while near the center the small round cells predominate.

Eye 23.—*Phlyctenule occurring in tuberculous rabbit at the height of a conjunctival reaction resulting from the instillation of tuberculin.*

Findings are essentially the same as in Eyes 35 and 16. The chief difference lies in the greater hyperemia and the smaller amount of proliferation of vascular endothelium.

A second phlyctenule which escaped clinical observation is seen in the conjunctiva at some distance from the corneal margin.

The foregoing report shows that in all of the phlyctenules studied the general structure is essentially the same. The lesion is composed chiefly of epithelioid cells and small round cells of the lymphocyte type. Over the summit of the nodule the epithelium is thinner than normal, at the margins it is thickened and irregular. Both in the cell mass and the overlying epithelium polymorphonuclear leukocytes are found. In detailed structure, however, the phlyctenules are sharply divided into two groups. In Eyes 31 and 48, in which the phlyctenules arose in the absence of local irritation from without, the epithelioid cells predominate, with relatively few small round cells. The endothelium of the capillaries shows little change. In the second group, including Eyes 35, 16 and 23, in which the phlyctenules accompanied a severe generalized conjunctival reaction, the epithelioid cells are much less numerous, being overshadowed by the greater number of small round cells. In this group the proliferation of vascular endothelium is a prominent feature.

The microscopic anatomy of these experimental phlyctenules bears a striking resemblance to that described by Weekers²⁹ and Hayashi³³ in human phlyctenular disease. Neither the human nor experimental phlyctenules show the typical changes of tuberculous tissue as evidenced by the presence of blood vessels and the absence of giant cells, caseation and tubercle bacilli. Yet there is reason to believe that they are tuberculous in origin. Weekers has pointed out the great similarity, both in their mode of occurrence and in their pathology, to certain types of tuberculids. In some of the tuberculids, whose tuberculous origin is extremely probable, no organisms have been found, and some of the features of typical tubercle are lacking. To these tuberculids the phlyctenule bears a close resemblance. Weekers believes that these atypical lesions result from the toxins of the tubercle bacillus rather than from the presence of the organism itself. The frequent occurrence of phlyctenules as a complication of the Calmette reaction, and their production experimentally in animals under similar conditions, lend weight to this view.

In addition to the phlyctenules themselves, an additional interesting condition was observed in Eyes 35, 16 and 23, in which a generalized conjunctival reaction was present. Although the phlyctenules were sharply circumscribed in a peripheral direction, they were not definitely limited in their extent along the limbus, there being a cell exudate of varying intensity throughout its entire circumference. This is shown in Figure 6, which represents a section of Eye 35 at some distance from the phlyctenule. To ascertain whether a similar cell infiltration was present in a conjunctival reaction even in the absence of phlyctenules, a tuberculous rabbit's eye was removed at the height of a conjunctival reaction in which no phlyctenules occurred. A similar cell collection at the limbus was found also in this case.

The character of the exudate differs, however, from that of the phlyctenule itself. The infiltration is composed of small round cells, and of cells about the size of polymorphonuclear leukocytes, having round or slightly oval, deeply staining nuclei and nongranular cytoplasm. The epithelium is not thinned, but in places is thickened and irregular. There are a few polymorphonuclear leukocytes in the cell mass. No necrosis is observed. The endothelium of the capillaries does not show proliferation. Why a cell collection should occur only at the limbus, notwithstanding the fact that the tuberculin comes in contact with the entire conjunctival surface, is not clear. Yet the fact is of special interest, inasmuch as the limbus is the most frequent location of phlyctenular disease.

Thus it is seen that in the phlyctenules occurring at the height of a conjunctival reaction, the clinical picture is that of a more intense

localized reaction superimposed on a generalized conjunctivitis. The pathologic picture is that of a dense localized cell mass superimposed on a cellular exudate of varying intensity which involves the entire circumference of the limbus. The findings do not accurately reproduce those found in human phlyctenular disease, in which sharp localization, both clinically and pathologically, is a distinctive feature. On this account the two instances in which phlyctenules occurred in the absence of local irritation from without are especially significant. For in these two cases the conditions under which human phlyctenules occur seem to have been exactly duplicated. The animals were tuberculous. No instillations had been made into the affected eye. There was no generalized conjunctivitis. The lesions were typical both clinically and microscopically. It is true that in Rabbit 31 tuberculin had been previously instilled into the opposite eye, and Rabbit 48 had received tuberculin subcutaneously. Whether the tuberculin had any influence in producing the phlyctenules it is impossible to say. The fact remains that the tubercle bacillus, or its toxins acting from within, seemed alone responsible for the occurrence of the lesions.

Save for the specific action of tuberculin, local irritation from without could not be shown to have any part in the production of phlyctenular disease. Organisms in the eye secretions showed no significant changes in number or variety. Of five cultures from the surface of the phlyctenules in Eye 31, taken immediately before enucleation, four were negative; the other showed a single colony of *Staphylococcus albus*. Careful search failed to reveal organisms of any kind within the lesions or on their surface. In early phlyctenules, whether human or experimental, the overlying epithelium is regularly found to be intact. Moreover, in human corneal phlyctenules examined by Hayashi²⁵ the cell mass was shown to lie beneath Bowman's membrane. In early cases, both Bowman's membrane and the epithelium were unbroken. The absence of even microscopic abrasions of the overlying tissues argues against the invasion of external organisms as a causative factor.

SUMMARY

Clinical observations on ninety-two cases of phlyctenular conjunctivitis revealed the presence of tuberculosis in ninety cases, as shown by a positive von Pirquet test. In the two giving a negative reaction, the diagnosis was doubtful. No other condition, either local or general, could be found with sufficient frequency even to suggest any direct influence in producing the disease.

Phlyctenules were produced experimentally in tuberculous rabbits in eight instances; six times as a complication of a conjunctival reaction resulting from the instillation of tuberculin, twice in the absence of

local irritation of any kind. Numerous attempts to produce the condition in animals not tuberculous were unsuccessful. The pathology of the experimental lesions was similar to that of human phlyctenules. The microscopic findings suggested a tuberculous origin. All clinical, experimental and pathologic evidence points to tuberculosis, and tuberculosis alone, as the cause of phlyctenular disease.

It is with great pleasure that I acknowledge my deep obligation to all who have assisted me in this study: to Dr. Joseph Brennemann for the general plan and personal supervision of the clinical investigations; to Dr. Brown Pusey and his associate, Dr. Robert Blue, for allowing me to use their material, and for much helpful advice; to Dr. Carl F. Bookwalter for examination of the nose, throat, ears, and sinuses; to Dr. A. I. Kendall and Dr. A. A. Day for valuable suggestions in the experimental studies; to Dr. J. P. Simonds for the pathologic examination; and to Mr. M. R. Waltz for preparation of the microscopic sections. The photomicrographs were made by Mr. F. T. Harmon.

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SURGICAL DISEASES OF THE URINARY TRACT IN CHILDREN

WITH SPECIAL REFERENCE TO THE VALUE OF CYSTOSCOPY *

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It is not generally recognized that children are subject to most of the urologic diseases common to the adult. A review of recent pediatric and surgical literature would lead one to believe that, excluding a few well recognized conditions (as vesical calculus, pyelitis and renal tumors), urinary diseases were very rarely encountered. However, as a result of clinical experiences and postmortem examinations, we are convinced that diagnosis, in affections of the urinary tract, is by no means accurate, and that, in consequence, many cases are overlooked.

The reasons for this are as follows: 1. Diagnosis in general is much more difficult in infancy and childhood. 2. We are deprived of the information obtained by a careful history. Too often we must be guided by fragmentary descriptions of symptoms given by parents or nurses. Unless the condition, therefore, is clear cut with characteristic symptoms (as in vesical stone), it may be impossible to differentiate, by ordinary means, bladder or renal diseases from other affections. 3. Palpation, unless performed under anesthesia, is rather unsatisfactory in children. Then again, palpation is, at times, unreliable as a diagnostic aid, for absence of enlargement of the kidney by no means excludes disease (as in early tuberculosis, and small renal tumors). 4. The modern methods of examination which are considered routine in the adult are seldom applied in the young. The latter probably furnishes the chief reason for the numerous mistakes and uncertainties in diagnosis in this field. Cystoscopy, ureteral catheterization, functional tests, and the roentgen ray have not supplanted the older, time-worn procedures. The subject of urology, in its newer conception, is given scant attention and rarely is reference made to the value of cystoscopy. A number of textbooks ignore these methods, a few describe them perfunctorily, with comments as to impracticality and difficulty. Instead of cystoscopy, it has been suggested that both kidneys be

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exposed and examined through lumbar incisions before attempting radical operative procedures. This, despite the fact that exploratory exposure of the kidney has often been shown to be of no value. At operation it has frequently been demonstrated that there may be no pathologic changes evident by inspection and palpation, and still serious disease be present (tuberculosis localized in the pelvis or papilla, renal calculus, etc.).

The object of this article is two-fold: first, to call attention to the feasibility of applying in the young in the great majority of cases, the same diagnostic procedures used in the adult, namely, cystoscopy, ureteral catheterization, roentgen ray, cystography, and the functional tests; and second, to the fact that surgical diseases of the urinary tract in infants and young children are not so uncommon as we are led to believe.

CYSTOSCOPY AND URETERAL CATHETERIZATION IN EARLY CHILDHOOD

Nitze¹ was the first to call attention to the use of cystoscopy and ureteral catheterization in children, having, in a few instances, successfully cystoscoped males as young as 8 years of age. In younger children where this examination was urgently indicated and the caliber of the urethra prevented instrumentation, a perineal urethrotomy was advised, through which the instrument could be passed. Casper² and Jacoby³ each described a child's cystoscope, but made no mention of its use clinically. Since then, few articles dealing with this subject have been published. This is probably due to the fact that up to a short time ago, satisfactory cystoscopes of small caliber were not available. At present, when such instruments can be obtained, but few clinics are supplied with the armamentarium necessary for these examinations. In females over 6 years of age, the ordinary adult cystoscope (21 French caliber) may safely be used, for the urethra possesses marked dilatability. In 1908, Portner⁴ described a new child's observation and catheterizing cystoscope and reported its successful use in a number of cases. The observation cystoscope has a caliber of No. 12 French, the catheterizing instrument No. 17 French. With these he succeeded in cystoscoping boys of 2, and catheterizing them at 8 years of age. Portner's cystoscopes were found to be unsatisfactory on account of the flexibility of their long shafts. Beer,⁵ in 1907, had two instruments made by the Kny-Scheerer firm (Reiniger,

1. Nitze: *Lehrbuch der Kystoskopie*, 1907, p. 97.

2. Caspar: *Handbuch der Cystoscopie*, Leipzig, 1911.

3. Jacoby: *Lehrbuch der Kystoskopie*, Leipsic, 1911.

4. Portner: *Deutsch. med. Wchnschr.*, 1908, No. 43.

5. Beer: *Cystoscopy and Ureteral Catheterization in Young Children*, *Jour. of Surg.*, March, 1911.

Gebbert and Schall), and published the results of his experiences with them a few years later. The catheterizing cystoscopes are Nos. 15 and 18 French, the observation instruments approximately 10.5 and 12.5 F. caliber. The shafts are made to fit the length of the urethra of a 5-year-old boy (8-10 cm.), and are 9.5 cm. and 12 cm. in length, respectively. Each is so constructed that the catheterizing sheath can be readily detached, making an examining and single catheterizing cystoscope in one. Both have an Albarran finger for guiding the catheter and take a No. 4 to 5 F. The optical system, which is modeled after Nitze, gives a very clear, though small, picture. With these instruments, Beer examined cystoscopically boys of 5 years, and girls as young as 14 months of age. The young child whose ureters were catheterized was a girl 5 years old. These cystoscopes have been in use since 1907 and have been found very serviceable, their great advantage being smallness of caliber and shortness of shaft.

We have records of more than thirty children under 9 years of age who have been cystoscoped during the past few years. The youngest patient was a boy of 17 months who was subsequently operated on for a kidney tumor. The youngest boy catheterized was under 3 years old — the youngest girl 22 months of age.

INDICATIONS AND CONTRAINDICATIONS FOR CYSTOSCOPY IN THE YOUNG

While cystoscopy in young children is devoid of danger, the indications for its application are not as broad as in the adult. The fact that a general anesthetic is required in most cases acts somewhat to restrict its use as a routine diagnostic procedure. It should be reserved for those cases in which surgical affections of the urinary tract are present; or as an aid in differentiating conditions which may be confused with diseases of the urinary organs. Care should be taken to rule out cases with urinary symptoms due to functional disturbances so frequently met with in young children (for example enuresis — hyperacidity of urine). Urinary findings unfortunately cannot be relied on to serve as a reliable guide on which to base indications. At times advanced lesions of the kidney may be present, and the examination of the urine give no intimation of the condition. A pyonephrosis with obstruction of the ureter on the diseased side may show an absolutely normal urine. Cases of congenital stricture of the ureter producing pyonephroses, with negative urinary findings have been reported from time to time in the literature.⁶ In tumors of the kidney also the urine frequently fails to contain any abnormal constituents. Pyelitis can generally be

6. Kahn: Congenital Stricture of Ureter Producing Pyonephrosis, *Med. Rec.*, New York, Nov. 16, 1912.

diagnosticated without cystoscopy, and should therefore contraindicate this examination. Every case of pyuria which does not respond to the usual methods of treatment, especially when accompanied by fever, loss of weight and strength, should be cystoscopically examined. Hematuria is also a distinct indication, unless it be proved that the bleeding is but an expression of a hemorrhagic diathesis (purpura hemorrhagica, hemophilia, leukemia, scurvy); or a hemorrhagic nephritis. Renal diseases are often simulated by intraperitoneal conditions; in these cases, cystoscopy is of great value in the differential diagnosis, and its application will often render unnecessary exploratory operations. Before deciding to remove a kidney no matter how badly diseased, the presence of the second should always be ascertained. Cystoscopy is not absolutely essential if the roentgen ray shows the shadow of the other organ. It is of great service when no focal renal symptoms are present, and the kidneys cannot be palpated, in determining the side of the lesion.

Contraindications have been mentioned in discussing pyuria and hematuria. In addition, when the child's condition is such as to preclude a general anesthesia, should this be necessary. Every case, however, must be considered by itself, and if there exists the slightest suspicion that cystoscopy will aid in the diagnosis, it should be used.

Functional test: When ureteral catheterization is not feasible, chromo-ureteroscopy will be found invaluable. It is possible by using this method to make a positive diagnosis in the majority of instances with the ordinary observation cystoscope. Indigocarmine (10 c.c. of 0.4 per cent. solution) is injected about fifteen minutes before the examination, and both meati carefully watched. First the time of appearance of the dye on each side is observed; then the intensity of the color, whether light or dark blue; and lastly, note made of the contractile force with which the colored urine is ejected from the orifice. The latter points are of great importance; a very light blue stream which simply dribbles away is indicative of disease. Normally, the dye appears in ten to fifteen minutes; its absence indicates grave renal impairment. When combined with catheterization, we have the additional data obtained by the examination of the separated urines.

The status of the other functional tests now in vogue has been summed up as follows by Leopold and Bernhard:⁷ "Figures for the nonprotein constituents of the blood as well as for the phenolsulphonephthalein excretion of children free from renal disease are practically identical with the figures obtained from adults, and vary within the normal figures as adult figures vary. The changes in these figures in

7. Leopold and Bernhard: The Nonprotein Nitrogenous Constituents of the Blood, and the Phenolsulphonephthalein Test in Children, *AM. JOUR. DIS. CHILD.*, 1916, **11**, 432.

children the subjects of renal disease correspond with the changes observed in adults. The importance of the tests for diagnosis and prognosis amply demonstrated in adults will in all probability, hold true for children." We have not used the phenolsulphonephthalein test in conjunction with cystoscopy and ureteral catheterization, but have confined its use to estimating the total functioning capacity of both kidneys.

TECHNIC OF CYSTOSCOPY AND URETERAL CATHETERIZATION IN CHILDREN

This does not vary much from the routine followed in the adult. Most cases must be examined under narcosis, and a deep anesthesia is generally required before the bladder reflexes are abolished. Occasionally it is possible in very young children, especially girls (3 to 4 years), to use the cystoscope under local anesthesia (novocain). The indigocarmin is injected ten to fifteen minutes before the anesthesia is started. It is often advisable to insert a small catheter into the bladder and wait until the color first appears in the urine before administering the anesthetic. The bladder is then irrigated with a small syringe, and filled with a sterile solution. The capacity of the bladder in a 1-year-old child is approximately 100 c.c., so that 120 c.c. is a safe amount for those over 3 years. As most of the catheterizing instruments for children are single tunneled, but one ureter can be catheterized at a time. It is seldom necessary to catheterize the two. A specimen from the diseased side is generally taken, and the excretion of indigocarmin from the other side noted; this suffices. Occasionally difficulty will be experienced (especially when using a No. 4 catheter) in obtaining a specimen; under such conditions, it is advisable to employ aspiration with a small syringe, or to inject a few cubic centimeters of sterile solution through the catheter, to start the flow.

Roentgenography.—In children, roentgenography is of greater diagnostic value than in the adult and should be used more frequently, especially in cases where the cystoscope cannot be used. Its importance lies in the fact that with good technic the outline of the kidneys can be distinctly shown and deviation in position, size and shape noted. It is at times possible to distinguish an intra-abdominal tumor from renal enlargement.

Cystography.—Roentgenographic studies of the bladder with silver salts, or thorium, is a harmless and often valuable procedure. In chronic vesical retention of urine in children, cystography aids materially in corroborating the diagnosis and in determining the degree of

involvement of the ureters and the kidneys. The bladder is filled with one of the solutions mentioned, the child placed in the Trendelenburg position, and roentgenographed. The roentgenogram shows distinctly in the more advanced cases the considerably enlarged bladder with dilated ureters and renal pelvis. Diverticulæ of the bladder are well shown in the cystogram, and a more accurate idea obtained of their size and shape than by cystoscopic examination. The diagnosis of this condition is practically impossible without recourse to one of the two methods mentioned.

In the examination of children suspected of urinary disease, it is advisable, as in the adult, to follow a certain routine. The different steps of the examination should be carried out in their proper sequence, thus avoiding unnecessary repetition. The following has been found the most satisfactory. 1, history; 2, physical examination; 3, urinalysis; 4, roentgenography; if cystoscopy is contraindicated, or cannot be performed — cystography; 5, instrumental examination, which may include bladder catheterization — the stone searcher, and cystoscopy combined with injection of indigocarmin. If cultures of the urine are desired, catheterization is advisable. It is seldom necessary to collect a twenty-four-hour specimen, a single one generally suffices. Roentgenography should include the entire urinary tract, not alone the side towards which suspicion is directed.

The material embodied in this paper is based on a group of thirty-eight cases from the children's surgical wards of Mount Sinai Hospital, and from private records.* The youngest patient operated on was a girl, 11 months of age. This point emphasizes the fact which has been noted in a number of instances, that young children bear major operative procedures on the urinary tract very well. One should not hesitate on account of the extreme youth of the patient to operate, provided the child is in fair condition. As an instance, I may refer to a case recently reported by Kakels,⁸ in which an infant, 6 weeks old, had a nephrectomy performed for a large congenital hydronephrosis. Operation was followed by an uninterrupted recovery.

The youngest patient in this group was 11 months old, the oldest, 13 years; the majority of the cases were in children between 4 and 8 years of age.

The series to be described by case reports illustrating the various points previously mentioned, comprises the following surgical diseases of the urinary tract.

*I wish to thank Dr. Beer for the use of his private records, which have been incorporated in this article.

8. Kakels: Large Congenital Hydronephrosis in an Infant Six Weeks of Age, *New York Med. Jour.*, March 18, 1916.

	Cases
Perinephritic abscess.....	4
Renal tuberculosis.....	3
Renal calculus.....	2
Ureteral calculus.....	1
Vesical calculus.....	1
Tumor of kidney (Wilms).....	2
Sarcoma of kidney.....	2
Pyelonephritis (unilateral).....	1
Pyelonephritis (bilateral).....	2
Hydronephrosis (congenital).....	1
Hydronephrosis (traumatic).....	1
Suppurative nephritis.....	1
Subacute nephritis.....	1
Diverticulum of bladder.....	1
Chronic vesical retention of urine.....	12
Nephroptosis.....	1
Perinephritis (nonsuppurative).....	1
Contusion of kidney.....	1

Perinephritic Abscess.—There were four cases in this series, the youngest an infant of 16 months. Two patients were cystoscopically examined, one a child 20 months of age. The urine was negative in all but one case in which pus and blood were present. The abscess in this instance was caused by the perforation of a cortical abscess of the kidney into the perinephritic tissue. At operation this could be definitely determined. Cultures from the pus in three cases showed *Staphylococcus aureus*, in the fourth *Streptococcus hemolyticus*. The diagnosis is not difficult, and is readily confirmed by aspiration. Cystoscopy is seldom required for corroboration. Incision and drainage effect a cure unless there is marked renal involvement. Two of the patients had crops of furuncles preceding the development of the perinephritic abscess.

REPORT OF CASES

CASE 1.—*Left Perinephritic Abscess.*—P. K., aged 3 years, had measles at 9 months; had furuncles on buttocks a few weeks prior to admission; these disappeared without surgical treatment. After fever, pain in the left loin, and vomiting, physical examination demonstrated a large, tender, fluctuating mass in the left costovertebral angle. On aspiration a thick pus was obtained. Culture showed *Streptococcus hemolyticus*.

Operation consisted of incision and drainage of the perinephritic abscess. The kidney was not explored; tube drainage was instituted. Recovery was uneventful. The patient was discharged from the hospital a few weeks later.

Renal Tuberculosis.—Tuberculosis of the kidney in children is considered a rare disease. Oraison,⁹ in 1913, called attention to the fact that but fifty-one cases had been published in the literature. Wildbolz¹⁰ collected 896 cases in which tuberculosis of the kidney, in a surgical form, was clinically recognized forty-eight times. Necropsy findings,

9. Oraison: Jour. d. Urologie.

10. Wildbolz: Chirurgie du Nierentuberculose, Neue Deutsche chirurgie, 1913, 6.

however, tend to prove that the condition is much more common than clinical statistics indicate. O. Muller¹¹ found renal tuberculosis thirty-three times in a series of 100 necropsies on tuberculous children, Dickinson,¹² forty-nine times in 300 cases; Rilliet and Barthez¹³ found 15 per cent. of 312 tuberculous children had renal involvement. The Berne pathologic institute reports thirteen cases, in a series of 126—almost 10 per cent.

These figures thus indicate that renal tuberculosis in children is not such a rare condition, and that the application of the modern methods of examination would bring more cases to light. In every suspicious case, the urine should be most carefully examined for tubercle bacilli, and if found negative, inoculated into guinea-pigs. In children up to 10 years, the miliary type of tuberculosis predominates; after this age more cases of the chronic cavernous caseating form are observed.

CASE 2.—Right Renal Tuberculosis.—T. K., a girl, aged 10. The patient had nocturnal enuresis since childhood. For the previous few years she complained of infrequent attacks of pain in the right loin, and for the previous ten months had incontinence and loss of weight.

A poorly nourished child; kidneys not palpable; urine cloudy; albumin ++; considerable pus; cultures negative; tubercle bacilli found in smears; roentgen-ray examination negative.

The cystoscopy and ureteral catheterization showed bladder capacity considerably diminished; around the retracted right ureteral orifice an exudate; left orifice normal; left ureter when catheterized, showed deep indigocarmine concentration in twenty minutes; catheter was left in situ and bladder catheter introduced to obtain a specimen from the right kidney. The urine through this catheter became dark blue in one hour; urine from left kidney contained a few white and red blood corpuscles, hyaline and granular casts; urea 2.4 per cent.; no tubercle bacilli. Bladder urine representing the right kidney revealed white blood corpuscles +++; few red blood corpuscles; urea, 1.8 per cent.; tubercle bacilli present.

March 3, 1915, nephrectomy for right renal tuberculosis revealed areas of caseating tuberculosis in the upper and lower poles. Incontinence, daily and nocturnal, stopped before the patient left the hospital; convalescence uneventful.

CASE 3.—Left Renal Tuberculosis.—I. G., 10 years old, had had measles and scarlet fever.

Eight months previous to admission the patient suddenly experienced difficulty in urinating, followed by great frequency and urgency, but no hematuria. The symptoms persisted for three months, then improved somewhat; for the previous three months, he had complained of pain on urination in the end of the penis; passed bloody urine a few times; no lumbar pain.

An anemic child, but otherwise negative. The kidneys were not palpable (under anesthesia). Rectal examination was negative. The urine was cloudy, acid, with many pus cells; albumin +.

11. O. Muller, quoted by Wildbolz: *Chirurgie du Nierentuberculose*, p. 4 (Footnote 10).

12. Dickinson, quoted by Wildbolz: *Chirurgie Nierentuberculose*, p. 4 (Footnote 10).

13. Rilliet and Barthez, quoted by Wildbolz: *Chirurgie Nierentuberculose*, p. 4 (Footnote 10).

Cystoscopy showed the retrotrigonal area inflamed and in places ulcerated. The left ureter was golf-hole shape; the right ureter was normal, covered with fibropurulent exudate.

Indigocarmin appeared from the right ureter in fifteen minutes, in good concentration. The left ureter was catheterized and purulent urine obtained; there was no indigocarmin secretion. Tubercle bacilli were found in the urine from the left kidney. Roentgen-ray examination showed the left kidney slightly enlarged and ptosed. Nephrectomy was performed later for left renal tuberculosis. An enlarged, adherent, tuberculous kidney was removed; caseating areas were found in the lower pole. Uneventful convalescence.

CASE 4.—Left Renal Tuberculosis.—H. H., aged 11 years, was operated on for abscess on the lower end of the spine eight months previous to admission. Four weeks previously the child noticed blood at the end of urination and pain in the end of the penis. Since then he had frequency, urgency and burning.

A fairly well nourished child; kidneys not palpable; marked kyphosis of the lumbar spine; urine acid; slightly cloudy; albumin +; many pus cells and red blood corpuscles; smears negative for tubercle bacilli.

Cystoscopic examination under ether showed the bladder inflamed in the retrotrigonal region; left ureteral orifice did not contract or emit urine; good indigocarmin concentration from the right kidney, which was readily catheterized; no flow from left kidney in thirty minutes; tubercle bacilli found in twenty-four hour specimen; roentgen-ray examination, negative; no enlargement of kidneys. Diagnosis: left renal tuberculosis.

The pathologic report after nephrectomy for left renal tuberculosis showed tubercle bacilli present in the kidneys. Uneventful convalescence.

Urinary Lithiasis.—Not until the advent of radiography was it realized that urinary lithiasis in infants and young children is not an uncommon condition. Before then, it is true, vesical stone was recognized for generations, and its surgical treatment accorded a prominent place in the literature. Renal and ureteral calculi were considered extremely rare, and this is not surprising in view of the fact, that the diagnosis without the Roentgen ray is most difficult. That the condition is frequently overlooked is seen by the statistics of Rafin.¹⁴ He reports a series of 322 cases of renal calculus in infancy; 139 were found at necropsy; 140 occurred in infants under 1 year, twenty-six in children from 1 to 5 years. The small calculi so often present in infancy may be the basis of further trouble in later years.

Vesical calculus is a rather common disease in certain localities. Bokay¹⁵ has collected 1,836 cases of stone in infancy and young children; 1,319 were vesical, one half were urethral, and nine were renal calculi. The diagnosis of vesical calculus offers little difficulty; the rather characteristic syndrome immediately fixes attention to this region. Rectal palpation should always be practiced, and has at times clinched the diagnosis. The stone searcher and cystoscope are valuable aids; the roentgen ray is most important of all. Renal and ureteral stone offer more difficulties; for this reason roentgen-ray examination

14. Rafin: Ann. d. Mal. d. Org. Genito-urinaire, 1911, 29, 481.

15. Bokay: Ztschr. f. Kinderh., 1912.

should be used in a more routine manner. The presence of sand and gravel in the urine of young children, abdominal pain, spasmodic in character and accompanied by vomiting, are sufficient indications for roentgenography. Roentgen-ray examination should include the whole urinary tract, for stones may be located simultaneously in both kidney and bladder, as in the case to be reported.

CASE 5.—Renal and Vesical Calculi.—A. S., a boy. Patient had had measles and paratyphoid fever. Five weeks before admission the child had a sudden attack of retention of urine, and was in another hospital, no diagnosis being made. Nine days before he complained of pain in the right side of the abdomen, very intense at times, but not radiating. There was no frequency or difficulty in urination; he vomited twice. The mother noted that the urine was cloudy.

A well nourished child; abdomen lax and tympanitic; a definite, small, tender mass deep in the right hypochondrium; temperature ranged from 102 to 104; urine amber, cloudy with a trace of albumin and many pus cells; cultures showed *Staphylococcus aureus*. On roentgen-ray examination a triangular shadow was found in the region of the pelvis of the right kidney, and another in the region of the bladder like a calculus. A second examination confirmed this, except that the shadow in the bladder region had moved.

A cystoscopic examination, under ether, showed a calculus on the floor of the bladder. Suprapubic cystotomy was performed. A stone the size of a cherry was removed.

The pelvis of the right kidney was opened and a triangular stone removed. Patient had a stormy convalescence, developing a bilateral otitis media; but was discharged well, with wounds closed.

CASE 6.—A second case of renal calculus was that of a child 6 years of age, whose chief complaint was nocturnal and diurnal enuresis. Roentgen-ray showed distinctly a calculus in the kidney. Cystoscopy was not done; operation was refused.

CASE 7.—Ureteral Calculus.—P. E., girl, aged 13 years. March 15, three months previous to admission had cramp-like, intermittent pain in the right lumbar region; no urinary disturbance, no fever, chills or hematuria.

Physical examination revealed a slight tenderness in the lower part of the right iliac region; otherwise negative. The urine was acid, clear, specific gravity 1.028. There were a few white blood corpuscles and a little epithelium. Roentgen-ray examination revealed two calculi present in the right ureter about 1 cm. from the orifice; phenolsulphonephthalein, 45 per cent. in two hours; no red blood corpuscles in centrifuged specimens.

Cystoscopy and ureteral catheterization performed; bladder negative except in the region of the right orifice, which was covered with mucopus; right ureter had an obstruction at 2.5 cm. which was finally passed and bloody urine obtained; no indigocarmin secretion in thirty minutes; in left ureter no obstruction; urine clear; good indigocarmin concentration in twenty minutes. Ureterogram of right ureter demonstrated shadows in the ureter. Extraperitoneal ureterotomy was performed; two stones were removed; convalescence was normal.

Tumors of the Kidney.—The growths most frequently seen in childhood are sarcomas and mixed tumors. The former are probably more common, and are of greater malignancy. The majority occur in early childhood; in a collection of 130 cases, 106 were found in the first five

years, and fifty-seven of these in the first two years of life.¹⁶ Pain is a prominent symptom in sarcoma and is generally severe, whereas in the mixed form, it is only complained of very late in the course of the disease. The tumors rapidly invade neighboring organs; cachexia is rapid. Recurrences or metastases are the rule. The mixed types of tumor (Wilms¹⁷) are supposed to take origin in embryonic tissue, and are entirely different from other renal growths. They are composed of collections of epithelium in the nature of tubular or glandular structures, and may contain besides smooth and striped muscle fibers, cartilage, fat, bone and proliferating connective tissue. The latter tissue is the one most frequently found. These tumors originate in the substance of the kidney, and grow directly into the parenchyma, but do not infiltrate as the sarcomas or carcinomas generally do. Clinically, they are characterized by their large size (at times filling almost the entire abdominal cavity), absence of pain, and apparent good health of the patient. Often there are no subjective symptoms, and the growth is not discovered until it has reached a very large size. Metastases are rare, although the tumors are exceedingly malignant. The urine usually shows no changes; hematuria when present, is generally microscopic. The disease is most frequently seen in early childhood; occasional cases in the adult are reported. In a series of 165 mixed kidney tumors, 131 appeared within the first 6 years of age. Bilateral cases occur; Walker¹⁸ reports ten instances in 141 cases. The prognosis is bad. Albarran¹⁹ places the mortality from recurrence after operation at 86 per cent., Walker²⁰ at 93 per cent.

CASE 8.—Tumor (Wilms) of Right Kidney.—J. M., boy, aged 17 months, fell down a flight of stairs three months previous to admission but sustained no contusions or lacerations; there was no bleeding. About two weeks later the mother noticed a hard mass in the abdomen. This increased in size, but was not painful. Occupying the right half of the abdomen was found a firm, elongated mass, smooth, dull to percussion; the free border extending to the right iliac fossa; seeming to be adherent.

The urine was cloudy, acid, no albumin, few white blood corpuscles and little epithelium. Roentgen-ray shows a homogeneous mass occupying the entire abdomen and part of the false pelvis; it could not be determined roentgenographically what this mass was.

Cystoscopy under ether showed the bladder normal; left ureter discharging concentrated indigocarmin; right ureteral orifice not distinctly seen; no indigocarmin from this side during period of observation; under anesthesia the mass felt nodular, movable and hard.

Nephrectomy for right renal tumor was performed. Normal convalescence; primary union. Pathologic report—Wilms tumor.

16. Holt: *Diseases of Infancy and Childhood*, 1903.

17. Wilms: *Mischgeschwulste*, Leipzig, 1899.

18. Walker: *Ann. Surg.*, 1897, **26**, 585.

19. Albarran and Imbert: *Les Tumeurs du Rein*, Paris, 1903, p. 443.

20. Walker: *Ann. Surg.*, 1897, **26**.

CASE 9.—A second case was that of a child, 3 years old, who had two large hard kidneys. Diagnosis before operation was, either bilateral polycystic kidney or sarcoma. The operation was more in the nature of an exploratory procedure; the sections removed were reported as Wilms tumor.

CASE 10.—*Sarcoma of Kidney*.—F. A., girl, aged 2 years, had pain in the right hypochondrium; no radiation; no difficulty or frequency of urination; mother noticed abdomen becoming larger.

Examination revealed a protuberant abdomen, with visible, hard mass in right upper quadrant, reaching 1 inch below the surface of umbilicus; surface smooth; axillary, cervical and inguinal glands enlarged. The urine was amber, acid, clear, specific gravity 1.016; moderate number of white blood corpuscles; phenolsulphonephthalein, 63 per cent.; urea, 10 mg. per 100 c.c.; urea, 36 mg. per 100 c.c.

Roentgen-ray examination revealed a large, dense, homogeneous shadow which occupied the entire right side of the abdomen, ending near the brim of the true pelvis. The shadow had the outline of an enlarged kidney.

Nephrectomy for sarcoma of right kidney showed the kidney firmly adherent in removing, parenchyma was torn and sarcomatous tissue expressed, radium applied through drainage tract for period of 4,067.5 mg. hours; recurrence and death some months after.

CONGENITAL HYDRONEPHROSIS AND HYDRO-URETER

This is not uncommon in infants and very young children. In a series of 500 cases²¹ of hydronephrosis which came to operation, fifty-one were in children 1 to 10 years of age. A large number are found at necropsy — the congenital hydronephrosis of the new-born. The diagnosis may at times be difficult, as is shown by the following cases.

CASE 11.—*Congenital Hydronephrosis*.—W. P., aged 3 years, boy, had malaria one year and measles six months previous to admission. Had poor appetite for a year, not gaining weight; for the previous ten days complained of hypogastric pains. His mother had noticed that the urine was cloudy.

Heart and lungs were negative; abdomen lax, tympanitic; no dulness, no masses palpable; urine cloudy, acid, specific gravity 1.020, with trace of albumin; many pus cells; negative for tubercle bacilli. Roentgen-ray examination showed the left kidney somewhat enlarged; right kidney normal. Cystoscopy under ether anesthesia showed bladder negative except for congestion in trigone, and slight swelling around the left ureteral region; indigocarmin seen emanating from right ureter in good concentration in fifteen minutes; none from left side in thirty minutes.

At a second cystoscopy one week later these findings were corroborated, and through a lumbar incision a considerably enlarged hydronephrotic kidney and ureter were removed; the ureter was the size of a small gut. Uneventful convalescence.

CASE 12.—Traumatic hydronephrosis occurred in a boy 10 years of age, appearing after the child had been struck by an automobile. A large tumor in the loin was noticed. Cystoscopy demonstrated absence of secretion from the right side; good function from the left. At operation a large hydronephrosis was found; nephrectomy; normal convalescence.

CASE 13.—*Diverticulum of Bladder*.—M. B., boy, aged 10 years, had had diphtheria at the age of 5. Five days before admission he had terminal hematuria, and pain on urinating; had occurred several times since; had some pain in hypogastrium, and felt he could not empty his bladder; slight tender-

21. Küster: Chirurgie der Nieren, Stuttgart, 1902.

ness in right costovertebral angle; right kidney palpable; hypogastrium filled by a globular mass not disappearing completely after urination; distended bladder; penile hypospadias; urine turbid; heavy trace of albumin; much pus and many epithelial cells. Phenolsulphonephthalein test gave color first in thirty-eight minutes; 45 per cent. excretion in two hours; residual urine 100 c.c.; cloudy; tubercle bacilli not found in urine; roentgen-ray examination negative.

Cystoscopy under ether showed the opening of a diverticulum in left bladder wall from margin of which indigocarmin issued; left ureter seemed open within the diverticulum, which was as large as a peach and the mouth of which was thrown into heavy folds.

There was a dilatation of the right ureter.

The diverticulum was found to compress both ureters, accounting for dilatation seen in roentgenogram. It was excised. The left ureter was found markedly distended and intimately adherent to sac, so that about 1 inch of its lower end had to be excised; the proximal end was then implanted into the posterior wall of bladder. Uneventful convalescence; bladder control excellent. Cystoscopy forty-seven days after operation showed the left (implanted) ureter in the median line, and functioning. Indigocarmin appeared in fair concentration in fourteen minutes; on right side in fifteen minutes; site of diverticulum not visible.

SUBACUTE NEPHRITIS

Surgery for this condition should not be undertaken unless all medical means have been tried for some time and found ineffectual. The Edebohls operation is not curative; it is usually undertaken for the relief of general anasarca, or for impending uremia. The patient in our series did not show any improvement after operation and succumbed within a few days. Koplik²² in 1911 reported a series of five cases in which the Edelbohls operation was performed, with marked improvement in four.

CASE 14.—*Subacute Nephritis.*—A. Z., girl, aged 6 years, was admitted with pronounced edema of eyelids, legs, neck, abdominal wall, and marked ascites; urine, 350 to 400 c.c. daily; many hyaline and granular casts; red and white blood corpuscles. The child did not respond to any form of treatment; edema persisted; urinary output did not increase; patient began to show signs of impending uremia.

On bilateral decapsulation the kidneys were found enlarged and beefy red; the condition gradually became worse, and the patient died two days later.

The diagnosis of this condition is simple and does not require instrumental examination. Despite the fatal termination of this case, numerous favorable reports have been published from time to time, and operation should always be considered, after all methods of treatment have failed.

CASE 15.—*Suppurative Nephritis and Perinephric Abscess, Congenital Stricture of the Meatus and Urethra.*—J. R., boy, aged 7 years, had had scarlet fever four years previous to admission; three years previous to admission had had an attack of difficult urination, with passage of blood and pus; one year later had a similar attack; the urinary stream was always small. Examination revealed tenderness and swelling in left lumbar region; temperature 103 F.;

22. Koplik: Tr. Assn. Am. Phys., 1911.

genital examination disclosed a pin point meatus; urine acid, cloudy, specific gravity 1.014, albumin ++, full of pus and red blood corpuscles. The diagnosis of a perinephric abscess was made, and the patient was immediately operated on. A large abscess containing thick pus was opened, the kidney exposed, and a perforation in the cortex felt near its middle; tube drainage; culture, *Staphylococcus aureus*.

A month later nephrectomy was performed for suppurative nephritis. The kidney was found completely disorganized and studded with multiple suppurative foci. Meatotomy was then performed and instruments up to F. 15 were passed. Uneventful recovery.

CHRONIC RETENTION OF URINE IN CHILDREN

Under this heading are included patients suffering from chronic vesical retention due to various etiologic factors. The condition receives but scant attention in the literature, sporadic cases being reported from time to time. Beer²³ recently published a series of nine cases, and calls attention to the fact that the disease is often unrecognized until a late stage has been reached. The clinical picture is fairly characteristic; the patients have the pale, pasty appearance of chronic nephritis. Difficulty of urination often accompanied by straining, is an early symptom. The bladder is regularly found distended, at times reaching above the umbilicus. Residual urine is present in large amounts. On palpation the bladder can be felt to contract and become hard. The urine is clear in the early stages, but as a rule, becomes infected later on. As a result of back pressure dilatation of the ureters and pelves develop; this can readily be demonstrated by thorium cystograms. Cystoscopy reveals a trabeculation of the bladder with patulous ureteral orifices. Functional tests demonstrate marked renal impairment. Neurologic examination of these patients often shows nothing abnormal, in others distinct evidences of spinal cord or brain lesions are found. In the neuromuscular type instruments pass readily into the bladder without encountering an obstruction. The etiologic factors have been tabulated by Beer as follows:

1. Mechanical obstructions: (a) extravesical, as congenital folds and strictures, including tight prepuce, small meatus, new growth. (b) Intravesical, as diverticulum of bladder, vesical stone.

2. Neuromuscular: (a) brain disease; (b) spinal cord disease; (c) spasticity of sphincter without definite neurologic signs, probably disease of spinal cord.

The prognosis varies with the type; when due to mechanical factors, surgical procedures are often curative. The neuromuscular group all terminate fatally, generally from renal infection and insufficiency. Operation is only palliative — cystotomy for bladder drainage — and nephrotomy when the kidney becomes infected.

23. Beer: Chronic Retention of Urine in Children, Jour. Am. Med. Assn., 1915, 65, 1709.

CASE 16.—Chronic Retention; Hypertrophied Bladder; Bilateral Hydro-nephrosis.—Boy, aged 15 months, with a globular tumor mass in the hypogastrium, always present except when emptied by a catheter; that is, distended, hypertrophied bladder. In the left lumbar region was a mass corresponding to the position of the kidney. This was probably a hydronephrotic organ. No neurologic symptoms were elicited.

Cystoscopic examination revealed bladder trabeculated; otherwise normal; no obstruction in urethra; indigocarmin did not appear until four and three-quarters hours after injection, which suggests a bilateral kidney involvement.

Diagnosis of chronic retention, hypertrophied bladder, bilateral (probably) hydronephroses, due to spasm of vesical sphincter.

PYELONEPHRITIS

It is often difficult, especially in the chronic forms, to differentiate between pyelitis and pyelonephritis. In fact, it has been claimed that there is always involvement of the renal parenchyma in pyelitis. In the acute stage, the clinical manifestations of a pyelonephritis are more pronounced; the fever is higher and remittent in character, and apt to be accompanied by chills; the local signs, tenderness and pain more marked. Pus is present in the urine in varying amounts depending on the location of the abscess. If in the cortex, pyuria may be absent or insignificant. Of considerable diagnostic aid in differentiating these conditions is the late appearance in the urine of blue colored pus after the administration of methylene blue or indigocarmin. Weeks, and often months, after, one or more specimens of urine may suddenly become stained blue, due to the rupture into the pelvis of parenchymatous abscesses which have stored the dye. Beer,²⁴ who first called attention to this phenomenon, described cases in which methylene blue was excreted as long as two and three-fourths years after its administration.

CASE 17.—Right Pyelonephritis.—P. T., a girl, aged 6 years; two months before admission had a bullous eruption on the body; one month later double otitis media and mastoiditis. The patient's urine had been cloudy for two years; complained of urinations every 1 to 2 hours for a few months; for the previous few weeks had had pain in right lumbar region; pain, tenderness and resistance in right flank; temperature fluctuated between 99 and 105 F.; no chills; urine is cloudy; specific gravity 1.020; full of pus; von Pirquet test, roentgen and tubercle bacilli negative.

On cystoscopy the bladder was found diffusely inflamed; the right ureteral orifice swollen, the left normal; both ureters catheterized; no obstruction; right kidney gave fair indigocarmin concentration in twenty-five minutes; catheter became clogged with pus; few cubic centimeters urine obtained; urea 1.1; many white blood corpuscles; left kidney gave good indigocarmin concentration in twenty minutes; urea 0.9; occasional white blood corpuscles.

The child was given large doses of hexamethylenamin. At intervals of two, three and six days, and two weeks following the injection of indigocarmin, after the urine had been clear, the blue color suddenly appeared in one or two

24. Beer: The Diagnosis of Pyelonephritis, Jour. Am. Med. Assn., 1907, 48, 1936.

specimens. The temperature gradually came to normal, and pus disappeared from the urine. Cystoscopic examination before leaving the hospital, showed very slight cystitis; no pus in catheterized specimen.

The other two cases of pyelonephritis in this series were bilateral, and occurred in female children 22 months and 4 years old, respectively. Both were catheterized, pus obtained from each kidney, and the colon bacillus found in culture in each instance.

CASE 18.—Retroperitoneal Tumor.—The following case is cited to illustrate the value of cystoscopy as an aid in differentiating an extravescical from an intravescical condition.

Six days before examination of a boy, 3½ years of age, a large mass was accidentally noted in the hypogastrium, which was hard, solid, nodular, extending from below the umbilicus well down into the pelvis. The question arose whether this tumor was a vesical or prostatic neoplasm or retroperitoneal growth. Cystoscopy demonstrated a normal bladder; both ureteral orifices were normal. Indigocarmine appeared in good concentration from both sides in twelve minutes. The diagnosis of retroperitoneal tumor was made.

CONCLUSIONS

Urologic diseases in children are not as infrequent as we are led to believe. Many of the cases in this series would undoubtedly have been overlooked had not the methods of examinations commonly employed in adults been used. The feasibility of cystoscopy in very young patients, and its practical value are amply illustrated by a study of the case reports. Too much stress should not be placed on negative urinary findings. Cystoscopy will at times be indicated despite the absence of abnormal constituents in the urine.

Of the functional tests, indigocarmine is the simplest in application, and is generally reliable. Its use, combined with the observation cystoscope, will often render catheterization of the ureters unnecessary. Phenolsulphonaphthalein and the blood tests (urea-nitrogen) are seldom indicated, unless from a prognostic standpoint. Roentgenography should be more frequently resorted to, and should precede every cystoscopic examination. In obscure vesical conditions, especially when cystoscopy is contraindicated or cannot be performed, cystography will often be found to give valuable information.

The proper application of the methods enumerated will seldom make it necessary to resort to exploratory operations on the urinary tract for diagnostic purposes. Operative procedures on the kidney, ureter or bladder are well borne in infancy and early childhood; in a series of over twenty-five major operations there was but one immediate death, that due to uremia following decapsulation for subacute nephritis.

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SEXUAL PRECOCITY IN THE MALE *

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CHICAGO

SYMPTOMS

In sexual precocity of the male we observe as the most striking feature a premature, disproportionate and excessive development of the genitals to the size of those of the full grown man, and also an early development of the secondary sexual characteristics, such as the growth of hairs ad genitalia, ad anum, in the axillae, on the face, and, to a lesser degree, on the remainder of the body, particularly on the extremities; the voice deepens, and in the majority of the cases an increased development of the whole body in length and width with a voluminous musculature (herculean type) and certain psychic features have been noted. This excessive growth, however, is only temporary and the final size of body is not abnormally large, but generally subnormal, since the ossification of the epiphyseal cartilages often occurs prematurely. Thus we observe somatically the ordinary signs of puberty, but at an abnormally early age. In a number of cases this or that symptom was wanting; occasionally there existed obesity.

Whilst in the female at the normal, as well as at the premature age, the time of the gradual onset of the new secretory functions of the sexual glands, that is, the expulsion of a mature ovulum can be determined more or less accurately, due to the accompanying process of menstruation, in the boy the time of the beginning of the secretory function of the sexual glands as manifested in nocturnal pollutions, ejaculations and spermatogenesis, remains as a rule unnoticed. However, the growth of the testes and the penis as a local sign of sexual ripening and the rapid development of the secondary sexual characteristics serve as a more or less reliable symptom of the approaching germinative secretion, the functional capacity.

According to Neurath's¹ publication, only in a few cases of precocity in boys described in the medical literature are to be found exact data as to the onset of emissions and ejaculations of semen.

White,² for instance, describes a case of a boy who, at the age of 2 years, practiced masturbation with resulting ejaculation of sperma.

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1. Neurath, R.: *Ergebn. d. inn. Med. u. Kinderh.*, 1909, 4, 46.

2. White: *Med. Chir. Trans.*, 1815, 1.

The 13-year-old boy, yet without crines pubis, reported by d'Outre-pont, impregnated a girl 9 years old, who still was without the slightest sign of puberty. This latter case demonstrates the well recognized possibility in the female of a very early ripening of impregnable ovula long before the onset of menstruation. Pellizzi⁴ in his cases likewise demonstrated the presence of spermatogenesis.

Definite data are also often deficient in the literature about the age in the boy at which the first symptoms of precocity appeared. According to the compilation by Neurath¹ in his monograph, the premature puberty in the male, as far as the respective ages were reported, was completed as follows:

	Cases
At the end of the first year.....	8
Within the second year.....	4
Third year.....	2
Third to fourth year.....	3
Fifth year.....	1
Fifth to sixth year.....	3
Seventh year.....	2
Eighth year.....	2
Tenth year.....	1
Twelfth year.....	1

In the majority of the more pronounced cases the excessive and rapid growth of the body had begun during intra-uterine life; whilst the premature and rapid development of the genitalia generally took place only some time after birth. On the other hand, sexual prematurity may commence during intra-uterine life, as boys and girls were born with unusually developed sexual parts that afterward continued developing.

In striking contrast to the premature development and excessive growth of the body in precocity is the persistence of the psychic functions in their infantile stage in most cases. Whilst under normal conditions at the period of physical puberty there sets in also a psychic one, a deep psychic alteration and transformation, a period of "storm and stress," often a tendency toward dreaming and reverie, this is not so in cases of prematurity. The children affected may be physically many years in advance of their age; the mind, however, corresponds, as a rule, to the real age; their behavior is childish, but the premature awakening of the *vita sexualis* lends it a peculiar color. Rarely does the psychic progress take place *pari passu*.

In other instances there exists a delayed mental development, a debility, imbecility or even idiocy, as in the cases of Moreau,⁵ Hofacker,⁶

3. d'Outrepoint: Quoted from Neurath (Footnote 1).

4. Pellizi: Quoted from Falta (Footnote 31).

5. Moreau: Jour. de méd. de chir. et pharmacol., 1806, 12, 274.

6. Hofacker: Naturforsch. Versammlung., Düsseldorf, 1903.

Hudoverning,⁷ Woods,⁸ Ziehn,⁹ Morse¹⁰ and the 2-year-old boy mentioned by Heller.¹¹ Of course, in case of pre-existing weakmindedness, neither in normal nor in premature puberty could any better development of the psychic functions be expected from these biologic processes.

In imbecille and idiotic children the genitalia more often are retarded (Heller) in their development, kryptorchism being here a very common manifestation of degeneracy. In precocious boys often there exist strong sexual impulses, and occasionally masturbation is mentioned. These facts call especial attention to the pelagologic side of the subject.

Excessive sexual impulses in early childhood may, in tainted neuropathics, exist previous to the anatomic development of the generative organs, and independent of physiologic processes; such sexual sensations, premonitions and impulses may then lead to severe masturbation and aggressivity. The occurrence of these isolated, excessive sexual impulses as a result of cerebral (central) processes without adequate peripheral causes represents a type of partial, namely, psychic precocity, included in the term "sexual paradoxia" (v. Krafft-Ebing) since they occur at an age when they should be absent. V. Krafft-Ebing, Féré,¹² Fuchs,¹³ Lombroso,¹⁴ Moll,¹⁵ Zambaco¹⁶ and others reported such cases. It is noteworthy that paradoxical sexual impulses have been observed also in animals. Weston¹⁷ reported a six weeks' old colt that used to spring on its own mother when 3 months old; on account of its sexual aggressivity it became so dangerous to other colts and calves that its castration was necessary. The author also mentions masturbation in a colt only 2 months old.

ANATOMY AND ETIOLOGY

Up to the compilation from the literature of Neurath¹ there were seventeen cases of postmortem and four findings during operations in both sexes; fourteen girls and seven boys. Five of these patients presented neoplasms of the sexual organs, ten or eleven demonstrated

7. Hudoverning-Popovits: Gigantisme précoce avec développement précoce, *Nouv. iconog. de la Salpêtrière*, 1903, **16**, 181.

8. Woods, T.: An Extraordinary Case of Early Puberty, *Lancet*, London, 1882, **2**, 377.

9. Ziehn: *Berl. klin. Wchnschr.*, 1906, p. 1095.

10. Morse: *Arch. Pediat.*, 1913, p. 179.

11. Heller, Th.: *Grundriss d. Heilpaedagogik.*, Leipzig, 1912, p. 172.

12. Féré: *Précocité et impuissance sexuelle*, *Ann. d. mal. d. org. génito-urin.*, 1906, No. 2, p. 1.

13. Fuchs, Alfred: *Jahrb. f. Psychiat. u. Neurol.*, 1903, p. 207.

14. Lombroso: *Arch. di Psichiat. [etc.]*, Torino, **4**, 22.

15. Moll, Albert: *Das Sexualleben des Kindes*, Berlin, 1907, p. 107.

16. Zambaco: *L'Encephale*, 1882, Nos. 1, 2.

17. Weston: Quoted from Moll (Footnote 15), p. 110.

neoplasms of the adrenals, three had tumors of the pineal gland; in one case (Wetzler) there existed hydrocephalus congenitus.

Very interesting is the case in which operation was performed by Sacchi¹⁸ for malign tumor of the testis. At the age of 5 years the boy's left testicle increased to the size of that in the adult, the body grew rapidly, the voice became deep, and hairs grew ad genitalia; at 6 years the development of the body was enormous; at 9 years of age the body length was 143 cm., the weight 44 kilograms; the beard was abundant. The left testis proved, after orchidectomy, to be an alveolar carcinoma. Four months after the operation the beard disappeared, the hairs on the upper lip and genitalia persisted. The voice became again infantile, the penis less large and thick, the sexual impulses, emissions and erections ceased; also the character reverted to the infantile stage.

These tumors of the genitive glands suggest that the irritation of the latter causes an excessive and premature increase of the function of the interstitial tissue of Leydig, hastening the development of the secondary sexual characteristics.

Bulloch and Sequeira¹⁹ compiled ten cases, eight girls and two boys, in which necropsy revealed tumors of the adrenals. One case of precocity in boys was the case of Linser,²⁰ in which a hypernephroma was found; the testes were of the size of a pigeon's egg and the prostate corresponded in size to that of a boy 15 years old. The other case, observed by Adams,²¹ was in a boy not yet 15 years old, who died one year later of metastases of hypernephroma. Later, Glynn²² brought the number up to seventeen cases in children; fourteen females and only three boys.

According to clinical and pathologic observations, we must ascribe to tumors of the adrenals merely a hastening influence on the development of the secondary sexual characteristics, causing also an excessive growth of the body, since other recognizable functions of the sexual glands, such as menstruation or ejaculation, are not mentioned in these reported cases. It seems that although the hyperfunctionary tumors of the cortex of the adrenals in the young give rise to greatly accelerated growth of the body and to premature development of secondary sexual characteristics, as a rule, it is so without any manifestation of a secretion of the generative cells. In such cases, with Tandler and Gross one might think of a premature function of the *Zwischensubstanz* without premature development of the germinative cells.

18. Sacchi: Riv. sper. di freniat., 1895, **21**.

19. Bulloch and Sequeira: Tr. Path. Soc., London, 1905, **56**.

20. Linser: Beitr. z. Klin. Chir., 1903, **37**, 282.

21. Adams, Ch.: Tr. Path. Soc., London, 1905.

22. Glynn: Quart. Jour. Med., 1912, **5**, 157.

In five cases, all boys, reported by Gutzeit, Cyrill Ogle²³ (sarcoma), Oestreich-Slawyk,²⁴ Frankl-Hochwart²⁵ and Raymond Claude,²⁶ post-mortems revealed teratomas of the pineal gland; Horrax's²⁷ case revealed at postmortem a struma of the pineal. It is not a mere coincidence, probably, that the pineal tumors were found only in *male* precocious children, whilst the adrenal hypernephromas are five times more frequent in the female than in the male.

The relation between genital hypertrophy and the pineal gland, according to Marburg,²⁸ is perhaps to be interpreted as due to a premature decrease of the functioning glandular tissue, which otherwise under normal conditions undergoes degeneration, beginning with the seventh year of life. The trophic disturbance, that is, the premature development, or as Pelizzi⁴ terms it, the macrogenitosomia praecox, may be considered as a manifestation of the insufficiency (*Ausfall*) of the epiphyseal gland. We have to presume that in childhood normally the pineal gland exerts an inhibitory influence on development, and that later the influence gradually diminishes and disappears, due to the partial involution of the gland. This interpretation of the premature development being due to hypopinealism finds its support in the results of experiments by Foa,²⁹ who, after extirpation of the epiphyseal gland in young roosters, observed a premature and excessive development of the testes and some secondary sexual characteristics.

The reports of positive findings made by Horrax²⁷ are in keeping with those of Foa.²⁹ The pinealectomized male guinea-pigs showed a hastened development of the sexual organs, manifested before maturity by a relative increase in size and weight, both of the testes and seminal vesicles, over control pigs of the same litter. The pinealectomized females appear to show a tendency to breed earlier than control animals.

On the other hand, extirpation of the generative glands in young animals has been followed by atrophy of the pineal gland (Biach and Hülles³⁰). The case of Marburg²⁸ also supports the supposition of the epiphyseal gland exerting an influence on the premature sexual development. The examination of the brain of the 9-year-old idiot with well developed crines pubis revealed a markedly inhibited development of the pineal gland, with entirely fetal cell-islands and a marked gliaplaque in its interior.

23. Ogle, Cyrill: Tr. Path. Soc., London, 1899, **50**, 4.

24. Oestreich-Slawyk: Virchows Arch. f. path. Anat., 1899, **157**, 475.

25. Frankl-Hochwart: Deutsch. Ztschr. f. Nervenhe., 1909, **37**.

26. Raymond-Claude: Bull. de l'Acad. d. méd., Paris, 1910, **63**, 265.

27. Horrax: Arch. Int. Med., 1916, **17**, 607, 645.

28. Marburg: Ergebn. d. inn. Med. u. Kinderh., 1909, **4**. Ibid., 1913, **10**, 146.

29. Foa: Arch. Ital. de biol., 1912, **57**, 233.

30. Biach and Hülles: Wien. klin. Wchnschr., 1912, No. 10, p. 373.

Marked hydrocephalus was found post mortem in the 8½-year-old girl reported by Wetzler. As early as in the sixth year of life menstruation took place, and the external genitalia were well developed and covered with hairs; uterus and ovaries had the size of those of a 20-year-old person. It is possible that this case belongs to primary hypergenitalism as well as a similar one of Pellizzi.⁴

Our positive knowledge of the etiology and pathologic anatomy is limited to those few cases. In a few observations premature sexual development has been ascribed to such early and excessive practices as masturbation and cohabitation due to seduction. Where such pathologic factors are absent, what the cause of the prematurity of the impulses for the somatic changes is remains a problem, as it is likewise not known why at a certain period of life under physiologic conditions certain organs should increase rapidly and perfect their function, the sexual glands particularly receiving impulses that cause a more rapid maturing. Though the nature of the primary stimuli that control these changes is not known, it is established that the endocrine glands in their interlocked and mutually affecting functions are of the greatest importance for the normal growth of the body and for sexual maturity, among them especially the genital glands, the adrenals, the pituitary body, the thyroid and the so-called "puberty-glands," the thymus and the pineal; their inextricable interaction in the main still defying analysis; the inner working of biologic laws, of the phylogenetic, hereditary and racial factors, of climate, etc., that regulate the onset of these processes remains obscure.

The following case of precocity was observed by me in the Cook County Hospital. The coincidence of imbecility renders the case more interesting and adds to the list of observations as exemplified by the reports of the authors before mentioned.

CASE REPORT

History.—K. W., 11½ years old, son of Ruthenian immigrants. The father is middlesized, of sturdy build, living at present out of Chicago; mother small. There were two other children with irrelevant histories. The patient was born at full term, weighed, allegedly, 7 pounds. He grew first slowly, more rapidly at 5 years of age; he has always been mentally much below par and somewhat hard of hearing, according to his mother's statement. He learns poorly, has a very poor memory and is in the first grade of the public school where he has attended for three years. He has had measles, scarlatina, diphtheria and whooping cough. He often snores and sleeps with open mouth. He began to grow rapidly about one year prior to this report; no information can be obtained from the mother about the sexual development of her boy; neither does she remember when he began to walk and talk.

Present Status.—The patient is of slender build, of blond type; height 1.51 m.; weight 85 pounds, with waist and coat off. The lower half of the body, measured from the lower edge of the symphysis to the heel, is 75 cm. The musculature is flabby and poorly developed; head rachitic, tubera frontalia and



Author's case of sexual precocity. Boy aged 11½ years.

parietalia prominent; fronto-occipital circumference, 55 cm.; there are twenty-eight perfect teeth; no trace of caries; chest poorly developed; chicken-breast deformity; circumference in nipple-line during middle respiratory position, 67.5 cm. The lower part of the abdomen is somewhat pendant, the muscles of the abdominal wall flabby and poorly developed. There is a slight degree of genu valga and beginning pedes valgi.

Genitalia.—In comparison with the age of the boy his genital organs are striking in their degree of development; there are also some secondary sexual characteristics present. The penis is 10.6 cm. long measured from the root at the symphysis to the end of the prepuce, and 9 cm. in circumference in the nonerected state. The prepuce reaches about 1 cm. beyond the glans. The testicles are of the size of those in the adult man, 3.5 cm. to 4 cm. long, the left larger than the right. There is an abundant growth of hair on the pubes, more than 5 cm. long; the upper border line is of feminine type; there is a conspicuous brown pigmentation of the median line from the mons veneris to the umbilicus. The scrotum is covered with a few hairs, 0.5 to 1 cm. long. In both axillae there are patches of skin of 1.5 to 2.5 cm. diameters that are covered with a crop of blond hair about 1 cm. long. The boy has vigorous erections of the penis, as was witnessed in the hospital. The prostate gland is of the size of that of an adult. Massage of the prostate and seminal vesicles, performed once, did not yield sperma. The larynx is very prominent, the voice strikingly deep.

The inner organs show no abnormal conditions; no tumor of the kidneys can be palpated, neither does roentgen-ray examination reveal any anomaly of these organs. The roentgenogram of the skull demonstrates a slightly enlarged sella turcica and a moderate increase in size of the skull. Roentgenograms of the hand show no deviation from the ossification that corresponds to the actual age of the boy. The ear drums are only slightly retracted, the hearing little affected.

Psychic Conditions and Habits.—The boy is very irritable; "nervous"; cries when his mouth is inspected. He is of a stubborn, disobedient, troublesome disposition, and resentful toward other children, and has to be reprimanded for it in the hospital. At home he prefers to play with boys younger than himself and shuns boys of his size; there are evidences of sexual shame; he chews his nails habitually; these are much bitten off. There seems to be at present no particular propensity to the other sex. He cannot count to more than five; even then he must be helped. He cannot write his name unless a copy is placed before him; his handwriting is hardly readable; nor can he do sums; he says for instance, 2 and 2 are 3, 2 and 2 are 6; 1 and 1 are 7. He is not able to say his prayers without being helped by his mother; he does not know any verses or any song, although he has attended, as mentioned before, the public school for three years. In fact, he is too dull to answer simple questions that refer to his own person, and during the examination he gives many evidences of a very poor memory even as to occurrences and experiences that would seem important to a normal boy.

Etiologically, the case may be classified as (primary) hypergenitalism without anatomicopathologic changes. The clinical examination excludes a tumor of the adrenals and there is no ground for suspecting a tumor of the pineal gland, corresponding cerebral symptoms being entirely wanting. Further, the makrogenitosomia praecox due to hypopinealism occurs only through premature destruction of functioning pineal tissue, that is, before the seventh year of life, since at that time the involution normally commences.

Against a hypophyseal affection (hyperpituitarism) militates the absence of such characteristic symptoms as were observed in the rare cases of acromegaly in adolescence and childhood. (Cases of Arnold, Claude, Schultze-Fischer, Hutinel, Pel and Salle, the two latter since birth. Quoted from Falta.³¹) The slight enlargement of the sella turcica hardly has any bearing in our case, considering the hydrocephalic increase in size of the skull of the boy.

4557 Broadway.

31. Falta, W.: *The Ductless Glands* (Translation from the German), p. 272.

PROGRESS IN PEDIATRICS

A REVIEW OF RECENT LITERATURE ON THE GENITO-URINARY DISEASES OF CHILDREN *

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VOLUME OF URINE

Addis and Watanabe¹ studied the daily volume of urine in adults on a standard diet and found that the volume of urine in any individual for any one day or part of a day is extremely variable in spite of constant water intake. They found that not less than 38 per cent. of the twenty-four hour volume was excreted during the first eight hours of the day, and not less than 53 per cent. in the first twelve hours. The night urine was never more than 47 per cent. of the total twenty-four-hour amount. Of course, the volume of urine excreted varies a good deal with the temperature, with the humidity, and with the number and character of the bowel movements, for if much fluid is excreted through these channels, there will be less excreted through the kidneys. Such studies are extremely valuable, as it is often necessary to know what the ratio between intake and output should be. As far as I know, no such work has been done with children, and it is rather difficult to decide sometimes in dealing with nephritic children, whether the urine output is as high as it should be in relation to the fluid intake.

CHEMISTRY OF URINE

C. U. Moore² discusses phenol excretion in the new-born and arrives at the following conclusions:

1. An increase in the number of stools per day is associated with a decrease in the total phenol output in the urine.
2. In a series of fifteen infants the phenol excretion per kilogram of body weight is less in the breast fed than in the artificially fed infant.
3. In infants and in adults, so far as it is possible to determine from the limited number of cases now at hand, there is an interrelation

* Submitted for publication Dec. 17, 1917.

1. Addis and Watanabe: Jour. Biochem., 1916, **27**, 267.

2. Moore, C. U.: JOUR. DIS. CHILD., 1917, **13**, 15.

between the total phenol excretion and the protein intake as measured by the total nitrogen excreted in the urine. This relation can be expressed in the general term "trebling the protein intake doubles the phenol excretion."

4. Contrary to the earlier findings, phenol is quantitatively present in the urine of every new-born infant, the average of nineteen cases being 11.2 mg. for the first three days of life.

5. As phenol is present during the period of starvation, it must originate in part through endogenous metabolism.

Johnson and Veeder³ have studied the nitrogen partition in the urine of normal children.

Urea nitrogen makes up from 80 to 85 per cent. and ammonia nitrogen from 3 to 5 per cent. The combined figure for the two is less than 90 rather than above 90 as in adults.

Creatin is constantly present, as is creatinin. The two combined form a smaller percentage than the creatinin alone in the adult. The amount of undetermined or "rest" nitrogen is high in children.

Torres⁴ discusses the relation between the diet and the acidity of the urine, and proves that a suitable regulation of the diet is a most valuable adjunct to the various drugs which have been used for the purpose. He arrives at the following conclusions:

1. The difficulties which one often encounters in changing the reaction of the urine in children are very much diminished when a suitable diet is prescribed.

2. Diminishing the amount of protein in the diet to 2 gm. and sometimes to 3 gm. per kilogram will often in itself render the urine alkaline without using a drug.

3. In cases in which the amount of protein reaches the lowest physiologic limit without turning the urine alkaline, one may continue to diminish the acidity by adding vegetables to the diet.

4. In cases in which vegetables are used to turn the urine alkaline, one must use, if possible, vegetables in which the amount of protein is smaller in proportion to the salts, like fruits, rice, wheat, etc., rather than those which have a large amount of protein, as peas, beans, etc. Substances which contain purins, like coffee, tea and cocoa, may increase the acidity, because they may produce uric acid.

5. In cases of infection, especially in infections of the urinary tract, and in cases of starvation, the urine tends to become more acid than in other conditions; therefore, it is more difficult to render it alkaline.

3. Johnston, M. R., and Veeder, B. S.: *AM. JOUR. DIS. CHILD.*, 1917, **13**, 404.

4. Torres, C.: *AM. JOUR. DIS. CHILD.*, 1917, **14**, 365.

6. When drugs are used without the proper diet, the doses necessary to make the urine alkaline are much larger than is ordinarily believed.

7. The action of drugs (either acid or alkaline) is very fleeting; therefore, they should be given in large and frequent doses.

ANURIA

Clough⁵ reports a case of prolonged anuria in a boy of 7. The boy had scarlet fever, and during the attack passed very little urine. When he came under the writer's care, soon after the attack, the anuria persisted, and for over a month he passed only from 2 to 6 ounces of urine a day. He never had any edema, nor any albumin, and on only one occasion were casts found in the urine. He made a good recovery.

CALCULUS

Lazelle⁶ reports a kidney stone in a child of 7. The symptoms consisted of attacks of abdominal pain, acute in character, passing off usually in a few hours. The roentgen ray showed a stone in the kidney, and at operation two stones were successfully removed.

While ureteral and kidney stones are by no means so common in children as they are in adults, they are not so rare as has been generally believed, and a number of cases have been reported of late years, particularly by English writers.

TUMORS

O'Neil⁷ says that bladder tumors in infants and children are distinctly rare. The great majority appear before the fifth year. They are of the connective tissue type, and are clinically and pathologically malignant, except in rare cases. Disturbances of micturition, shown by sudden retention or incontinence, are usually the earliest symptoms. Abdominal pain is a common symptom. The urine at first may show no abnormality; later signs of cystitis develop. As they do not tend to ulcerate at first, hematuria is often absent.

Early diagnosis and operation offer the only means of recovery.

Friedlander⁸ reports a sarcoma of the kidney treated by roentgen ray. The tumor occurred in a boy of 4 and was so large that no surgeon was willing to attempt its removal. Roentgen-ray treatments were started and for a while the tumor grew smaller, but later increased in size. The child finally died of bronchopneumonia occurring during an attack of measles.

5. Clough, F. E.: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 367.

6. Lazelle: *Northwest Med.*, 1916, **15**, 403.

7. O'Neill: *Boston Med. and Surg. Jour.*, Dec. 9, 1915.

8. Friedlander: *Tr. Am. Ped. Soc.*, 1916, **28**, 59.

The tumor examined at necropsy showed extensive degenerative lesions due to the roentgen ray, proving that the treatment was not without its effect on the tumor tissue.

ENURESIS

But little of importance has been written about enuresis recently. The very multiplicity of drugs and other measures that have been suggested to control this disorder show how little is really known about it.

Dunham¹¹ is an advocate of suggestion as a therapeutic measure in nocturnal enuresis. The condition, he believes, is not so common as is generally thought. Among 800 nervous children admitted to the Phipps Psychiatric Dispensary, ranging in age from 5 to 16 years, only 7 per cent. were bed wetters.

Many cases are due to pure nervousness and no abnormality of the urine or of the genito-urinary tract can be shown.

Dunham reports good results with his suggestive treatment, which he carries out as follows:

These four sentences are printed on a card.

1. I am not going to wet the bed.
2. I am going to wake up at midnight.
3. I shall get up and pass water.
4. I shall not wet the bed any more.

PYELITIS

R. M. Smith¹² discusses the mode of infection.

In favor of the ascending theory are the clinical data. Against it are the facts that colon bacilli have never been shown to pass up the normal unobstructed ureter, and that they have frequently been introduced into the bladder without causing any damage. He believes that the ascending theory has not been proved, and that the facts, experimental and otherwise, are against it.

The usual mode of infection is through the lymphatics, the colon bacilli invading the lymphatics from the intestinal tract, or from some focus elsewhere (particularly the vulva, in girls). From thence they pass into the blood, and from the blood to the kidney. After reaching the kidney they pass through the glomeruli and are excreted at the pelvis. They may be excreted without any damage, or may cause a pyelitis. Smith cites the case of a child who had a severe pyelitis secondary to a few impetiginous pustules on the neck. The cultures from the neck and from the urine showed *Staphylococcus aureus*.

11. Dunham, F. L.: AM. JOUR. DIS. CHILD., 1916, **12**, 618.

12. Smith, R. M.: AM. JOUR. DIS. CHILD., 1916, **12**, 103.

When the original focus of infection cleared, the pyelitis cleared up also. Smith explains the greater frequency of pyelitis in girls than in boys by the fact that the vulva, urethra and vagina are fine culture grounds for bacteria, which enter the lymphatics, blood, and finally the kidney, but that the infection does not ascend through the urethra.

Huet¹³ likewise supports the theory of descending infection. He reports an epidemic of pyelitis which started in a child who had pyelitis secondary to a bronchitis. Four other children who were cared for by the same attendant later developed pyelitis. He believes it was transmitted by milk: that the attendant in changing the babies' diapers infected her hands and then the milk. The colon bacilli recovered from all the cases were of the same type, and Huet believes that this series of cases proves that occasionally, at any rate, infection may be per os.

Helmholz and Beeler¹⁴ injected sixty-six rabbits with various strains of colon bacilli, and only two showed a typical pyelitis. Eleven rabbits were injected with a mixed culture of pneumococci and colon bacilli; of the eleven animals, six showed focal lesions of the kidney: three had pyelitis, one had cortical abscesses and two had diffuse hemorrhages into the cortex. Their conclusions follow:

1. It is possible to produce typical pyelocystitis in the rabbit by the intravenous injection of colon bacilli isolated from human cases.
2. If a mixture of organisms is injected, the relative number of kidney infections can be greatly increased.

Abt¹⁵ brings up the point that sometimes in a case of pyelitis several specimens of urine have to be examined before any pus can be found. He tends to favor the ascending theory of infection, because it is so well supported by the clinical facts. *Fever* and *restlessness* are the two main symptoms. Forcing water is the most important single thing in the treatment. Abt recommends using very small doses of hexamethylenamin and believes the patient should be watched very carefully while taking it. He does not favor the vaccine treatment.

Levy and Strauss¹⁶ find that the strength of formaldehyd necessary to inhibit the growth of the colon bacillus is a concentration of 1 to 5,000 or greater. Under a dose of 7 grains of hexamethylenamin three times a day (in adults) formaldehyd is never present in a concentration greater than 1 to 5,000. The only organism destroyed or inhibited by this concentration is the typhoid bacillus. For the destruction or inhibition of other organisms a high acidity of the urine is necessary, and this high acidity in combination with formaldehyd may produce injury of kidney tissue.

13. Huet: *Jahrb. f. Kinderh.*, December, 1915.

14. Helmholz, H. F., and Beeler, C.: *AM. JOUR. DIS. CHILD.*, 1917, **14**, 5.

15. Abt, I. A.: *Med. Clinics of Chicago*, 1916-1917, **2**, 895.

16. Levy and Strauss: *Arch. Int. Med.*, 1914, **14**, 730.

Graves¹⁷ discusses pyelitis with special reference to its occurrence in boys. He believes in the descending theory of infection. In the treatment of all cases of pyelitis in boys the intestine is to be recognized and dealt with as the potential source of the disease. The alkaline treatment is the best to follow in most cases. In all obstinate cases, autogenous vaccines should receive a trial.

Summary.—I believe at the present time it is fair to state that most authors favor the descending theory of infection. Opinions differ a good deal as to modes of treatment. Most agree that forcing fluid is of a good deal of value, and that vaccines may help somewhat in occasional chronic cases, but the relative virtues of the alkaline and of the acid-hexamethylenamin treatment have by no means been decided. A man of as great experience as Still recommends the alkaline treatment unreservedly, and barely mentions hexamethylenamin, and yet we know there are many cases of pyelitis which do not respond at all to alkalies. From what various men have written, it would seem that the alkali method of treatment will cure a good many cases, and that it is probably to be preferred to *small* doses of hexamethylenamin. Large doses of hexamethylenamin will, however, clear up many cases that have not responded well to small doses or to the alkali treatment. Such large doses are not entirely without danger, however, although by no means as dangerous as many writers state. The most reasonable method of treatment usually to follow, would, therefore, be to start with alkalies, and if good results are not apparent in two or three days, to use large doses of hexamethylenamin.

ORTHOSTATIC ALBUMINURIA

Jeanneret¹⁸ thinks that "postural" albuminuria is the best name for the condition, as other factors besides orthostasis enter into its production. He studied the effect of lordosis and of various postures in causing albuminuria in 204 children. His results may be summarized as follows:

1. Many children with a fixed lordosis have no albuminuria.
2. In only 3 per cent. of the children studied could albuminuria be induced by causing the patient to be in an artificially lordotic position, and then only if the child was kept motionless.
3. Orthostasis alone caused albuminuria in only 1.3 per cent. of the children, and then only when the child was kept motionless. Therefore neither lordosis *alone*, nor the erect posture *alone* is enough to produce albuminuria.

17. Graves: Am. Jour. Med. Sc., 1917, **154**, 548.

18. Jeanneret: Arch. de méd. d. enf., 1915, **18**, 46.

4. Lordosis and orthostasis combined, accompanied by movements of the legs, produced albuminuria in only 1.6 per cent.

5. The combination of the factors lordosis, orthostasis and immobility caused albuminuria in 49 per cent.

6. Sex, age and tuberculosis were found to have no etiologic significance.

Therefore, postural albuminuria is due not to a single factor, but to a combination of several.

When a child with a lordosis stands erect there is caused considerable venous stasis in the region of the kidney. Muscular contractions compensate for this by compressing the veins and helping the blood along with the aid of the valves, which are particularly numerous in the veins of the lower leg. If the muscular contractions are not vigorous enough, they do not suffice to compensate for the venous stasis that is caused by the lordosis and orthostasis, and albuminuria results.

These considerations are important in treatment. Nephritic albuminuria tends to disappear under the influence of rest; postural albuminuria tends to disappear under the influence of exercise, particularly of walking. This same exercise will exaggerate a nephritic albuminuria. Jeanneret believes, therefore, that children with postural albuminuria should be taken out of school for a few weeks, should be sent to the country, if possible, and made to exercise a great deal: in a word, exercise should be the specific remedy for postural albuminuria. The diet need not be restricted. The prognosis is excellent, and postural albuminuria never develops into nephritis. This is the most comprehensive study of the subject since that of Jehle, whose elaborate monograph appeared in 1909. Jehle believed that lordosis was the cause of albuminuria; Jeanneret seems to have proved that other factors are of equal importance.

Achard¹⁹ calls especial attention to the fact that orthostatic albuminuria often first appears after infections which may have affected the kidneys. He believes that in orthostatic albuminuria the lordosis and the orthostasis are acting on an already damaged kidney. In the normal subject the erect attitude diminishes the ease with which the blood returns by the inferior vena cava and the renal veins. There results from this the passage of a certain amount of fluid from the vessels into the lower part of the body, and an increased concentration of albumin in the blood, which can be demonstrated by the refractometer. At the same time there is a transitory diminution of the arterial pressure, and of the volume of urine. Lordosis facilitates venous stasis and the transudation of albumin, but something else is necessary in order to

19. Achard: *Rev. gén. de clinic et de therap.*, 1916, **30**, 625.

bring about albuminuria, and this additional factor is a slightly damaged kidney. The therapeutic indications follow these etiologic lines. Achard recommends neglecting the damaged kidney and treating the lordosis. It is the weight of the head and of the trunk which causes lordosis, because they are insufficiently supported by feeble muscles. The following measures he believes of value in treatment:

1. Resting in a prone position two hours after dinner each day.
2. Avoiding attitudes that provoke lordosis.
3. Special exercises designed to strengthen the back muscles.
4. Massage and hydrotherapy for the general circulation.
5. Diet and general hygiene.

Janeway²⁰ discusses especially the diagnosis as follows:

First put the patient to bed for a considerable period, to make sure that the urine becomes free from albumin after a reasonable length of time. The second specimen passed after going to bed ought to be albumin free, or we are not dealing with a case of postural albuminuria. After determining that the urine is free from albumin while the patient is flat on his back, we can have him stand in a markedly lordosed position against a wall for half an hour. This will usually produce extreme albuminuria, and on going to bed again the albumin will promptly disappear. Lordosis is an important, but not an essential factor; a considerable degree of lordosis may exist without albuminuria, and the albuminuria may exist without lordosis.

One interesting diagnostic point, according to Janeway, is that the majority of nephritics show only albumin coagulable by heat; orthostatic cases often show protein precipitated by acetic acid in the cold, which may be euglobulin.

The treatment consists in a correction of the posture, invigorating exercises and a full diet.

Barber and Smith²¹ made phenolsulphonephthalein tests on six patients with orthostatic albuminuria. In four cases it was quite normal. In one case it was 5 per cent. lower than the usually accepted standard. In the other case it was 14 per cent. lower with the patient standing than it was when made in the recumbent position.

Hempelman²² likewise investigated kidney function in orthostatic albuminuria by means of the phenolsulphonephthalein test. He found that the percentage of phenolsulphonephthalein excreted in two hours by normal individuals was not affected by position. In seven cases of orthostatic albuminuria the phenolsulphonephthalein test was from 58 to 86 per cent. When these patients were put in a lordotic position, producing a marked albuminuria, the total output of phenolsulphonephthalein in two hours was reduced on an average of 12.9 per cent.

20. Janeway: *Med. Clin. North America*, 1917, **1**, 21.

21. Barker and Smith: *Am. Jour. Med. Sc.*, 1916, **151**, 44.

22. Hempelman, T. C.: *AM. JOUR. DIS. CHILD.*, 1915, **10**, 418.

Beifeld²³ reports a case of orthostatic albuminuria cured by tonsillectomy and believes that chronically infected tonsils may occasionally be a contributing factor in causing the condition.

NEPHRITIS

The literature on nephritis in the adult in the last few years is enormous, but comparatively little has been written about the condition in children. Certain of the papers which have been written with especial reference to adults apply equally well to children, and for that reason a few of the more important ones are included here. Two things especially have interested investigators of nephritis in recent years, the functional capacity of the organ, and the classification of the different types of the disease. It is beginning to be realized that an accurate knowledge of the function of the kidney as a whole is more important to the clinician and to the patient than a knowledge of the particular type of damage that has been done to the various unit structures of the kidney as seen under the microscope, and for this reason pathologic studies have largely given way to chemical studies concerned with the power of the kidney to do its work.

The classification of nephritis has always been a most perplexing problem, and has never been very satisfactory. At present, authorities on the subject seem to be departing further and further from the old anatomic classifications, which recognized several types of both acute and chronic nephritis, and are tending to simplify the classification more and more, recognizing particularly clinical types of the disease rather than histologic types as shown under the microscope. This puts a complicated subject on a much simpler and clearer basis.

ETIOLOGY

Loeb²⁴ calls especial attention to tonsillitis as an important cause of nephritis.

1. Acute nephritis results from acute tonsillitis far more often than is usually believed.
2. The symptoms are not manifested until some time after the inception of the disease.
3. There are probably many cases in which a mild nephritis occurs incident to a tonsillitis, which goes on to resolution without the patient or physician being conscious of its presence.
4. It is incumbent on practitioners to examine the urine of every patient with tonsillitis, not only during the height of the disease, but for some time afterward as well.

23. Beifeld: *Jour. Lab. and Clin. Med.*, 1917, **2**, 638.

24. Loeb: *Tr. Am. Laryngol., Rhinol. and Otol. Soc.*, 1910, p. 146.

5. Spontaneous, or "idiopathic" nephritis is probably often due to a tonsillitis that has not been considered as an etiologic possibility.

6. Chronic affections of the kidney may very well owe their origin to unrecognized acute attacks of nephritis of tonsillar origin.

7. Much light may be shed on this subject by a study of the urine in a large number of cases of acute tonsillitis.

Grulee and Gaarde²⁵ discuss involvement of the kidney as a result of focal infections, with especial reference to tonsillitis. They report six cases of acute hemorrhagic nephritis in children, following several days after an attack of acute tonsillitis. The urine is very bloody, almost as to suggest a hemorrhage into the bladder. There may also be a good many pus cells present, the pus cells tending to appear as the reds diminish in quantity. There are no uremic symptoms, no edema, and the condition is usually much improved or entirely cleared up in two or three weeks. Cultures from the throat agree in many cases with the urinary cultures (hemolytic streptococci or staphylococci). In some cases the removal of a focus of infection such as the tonsils is followed by an immediate clearing up of the urine.

Baxter²⁶ reports five cases of acute hemorrhagic nephritis secondary to infection of the post nasal space. Symptomatically, the children became well in about four weeks, but the ultimate clearing up of the urine took from two to four months in some cases.

Dick and Dick²⁷ made urine cultures from a number of cases of chronic nonsuppurative nephritis, with the following results:

In all cases examined the urine contained numbers of bacteria, mostly anaerobes. In one case the bacterial flora of the urine was the same as that of a focus of infection in another part of the body. The bacteria isolated from the urine readily produced experimental nephritis. These facts lead us to believe that bacteria multiplying in the foci of infection frequently gain entrance to the blood stream and are excreted in viable condition through the kidneys, and that the excretion of bacteria in this way by the kidneys may be a common cause of nephritis.

The same authors²⁸ investigated a number of patients with evident focal infections to learn how frequently bacteria found in the focus of infection could be isolated from the urine, in what number they occurred in the urine, and whether excretion of bacteria might occur to any extent without clinical evidence of injury to the kidneys.

Eighteen patients were studied. In six of these the bacteria found in the urine did not correspond to those found in the focus of infection. In four cases a partial correspondence was found between the bacterial

25. Grulee and Gaarde: *Jour. Am. Med. Assn.*, 1915, **65**, 312.

26. Baxter: *Arch. Pediat.*, 1916, **33**, 729.

27. Dick and Dick: *Jour. Am. Med. Assn.*, 1915, **65**, 6.

28. Dick and Dick: *Arch. Int. Med.*, 1917, **19**, 493.

flora of the urine and that of the focus of infection. In eight cases the correspondence was more striking.

Staphylococci and gram-positive anaerobic diphtheroids are common inhabitants of the urethra. In eight cases, aside from these organisms, one or more of the kinds of bacteria found in the urine were isolated from the focus of infection.

Such studies indicate the very great importance to the kidney of focal infections.

Frank²⁹ believes that most nephritides in childhood are secondary to acute infection of some sort elsewhere in the body. There are, however, types of nephritis in infancy that are apparently primary, and are not dependent on previous infection. In babies, gastro-intestinal disease is often a cause of nephritis. Frank calls especial attention to the fact that of twenty-two cases investigated by him pathologically, many were of the hemorrhagic type, which is a particularly common sort of nephritis in childhood.

CLASSIFICATION AND GENERAL CONSIDERATIONS IN NEPHRITIS

Langstein and Benfey³⁰ adhere closely to the earlier classification of Heubner. They recognize the following types of chronic nephritis in children:

1. Chronic hemorrhagic nephritis is particularly characteristic of children. It is characterized by occasional exacerbations of hematuria, and nearly always is accompanied by edema.

2. A second form is first shown by edema, but is accompanied by no blood in the urine. The urine contains a great deal of albumin and many casts. Infectious processes are likely to be the cause of the nephritis in the first group, and not so likely in the second.

3. Contracted kidney, or "interstitial" nephritis (very rare).

4. A parenchymatous nephritis secondary to pyelitis.

5. A form of nephritis coming on very insidiously and manifested by general debility of the child, called by Heubner "paedo nephritis levis." The urine contains a small amount of albumin, a few casts and leukocytes, and from time to time a few red blood cells. It is very likely to be a sequel of scarlet fever or tonsillitis.

6. "Intermittent" albuminuria. Rare and of little practical importance.

Christian³¹ discusses the classification of chronic nephritis in adults. It is especially instructive to observe how he has done away with the old complicated anatomic classification. He says:

29. Frank: Arch. f. Kinderh., 1914, **11**, 202.

30. Langstein and Benfey: Med. Klin., 1914, **23**, 5987.

31. Christian: Cleveland Med. Jour., 1917, **16**, 223.

As our knowledge stands today, it is wiser to drop the terms "interstitial," "parenchymatous," etc., very largely from our clinical classification, and to use instead simple descriptive terms which indicate with the chronic nephritis the presence or absence of hypertension or myocardial insufficiency. The old type of kidney classification has been based on a study of the end-result of the diseased process.

Porter³² discusses the condition known as renal infantilism. This is a most interesting condition, which has been described by the English writers particularly. It is dependent on a contracted kidney with high blood pressure, of the same characteristics as so-called "interstitial" nephritis in the adult. Coexistent with the kidney condition is a state of infantilism. Porter's patient was 7 years old and weighed only 32½ pounds (should be about 49 pounds). There was incompleteness of calcification in all diaphyses, ossification was absent in the wrist bones, and the mental development corresponded to the stature of the child rather than to his age. He was very thirsty and passed a large quantity of urine of low gravity, containing a small amount of albumin and a few granular casts in the sediment. The bladder was of enormous capacity and he often voided 16 to 18 ounces at once.

The most striking symptoms in all the cases previously reported (looked up by Porter) were polydipsia, polyuria, enuresis and dry skin.

Parkinson³³ reports a case of nephritis without albuminuria. The child was 3½ years old, and had pneumonia, after which edema appeared. The urine showed no albumin, but microscopically showed a few red blood cells and casts.

He brings up the point that "latent" nephritis may be more common than is suspected.

It is doubtful whether such a condition should be called true nephritis. It corresponds rather to the condition spoken of as "acute renal irritation" which may occur in any acute fever. The pathologic text-books speak of it as "acute degenerative" nephritis.

H. Wessler³⁴ found that in nearly all of his nephritic cases in children, both acute and chronic, there was a distinct cardiac hypertrophy, often coming on as soon as two weeks after the onset of the nephritis. This was shown by percussion, by the fluoroscope and by roentgenograms.

Berkley and Lee³⁵ after a study of ninety-three cases of acute and chronic nephritis in children, have settled the question of blood pressure, which is one that had previously been in dispute. They found:

32. Porter: *Arch. Pediat.*, 1915, **32**, 85.

33. Parkinson: *Brit. Jour. Child. Dis.*, 1916, **13**, 138.

34. Wessler: *Arch. Int. Med.*, 1914, **14**, 516.

35. Berkley and Lee: *AM. JOUR. DIS. CHILD.*, 1917, **13**, 354

1. The blood pressure is elevated in the nephritis of childhood, and occasionally to a marked degree. This applies to both acute and chronic nephritis.

2. Systolic and diastolic pressures are not increased to the same extent, the former averaging about 20 mm. Hg, and the latter about 10 mm. above normal.

3. The pulse pressure is increased, but the factor is not constant.

4. The blood pressure in chronic nephritis shows no constant elevation above that in acute nephritis.

5. The blood pressure may, in rare instances, be of prognostic value.

6. No relation has been found to exist between the blood pressure and the urinary findings.

7. Patients having marked edema showed a slightly higher average blood pressure than those with little or none. The difference is not great enough to warrant any definite conclusions.

8. Albuminuric retinitis is probably not common, even in cases showing a marked increase in blood pressure.

FUNCTIONAL TESTS

Kidney function in children has not been investigated so extensively as it has in adults.

Leopold and Bernhard,³⁶ in a series of children free from renal disease, found that the phenolsulphonephthalein excretion for two hours varied between 50 and 96 per cent., with an average of 70 per cent. Five cases of acute nephritis and five of chronic nephritis were studied. In both the acute and chronic cases the phenolsulphonephthalein excretion was diminished. The same authors found in normal children the following apportionment of the nonnitrogenous constituents of the blood. The total nonprotein nitrogen varied between 19 and 40 mg.; the urea nitrogen varied between 8 and 21 mg., the average being 12 mg.; the uric acid varied between 6 and 3.2 mg., the average being 1.8 mg. The creatinin varied between 0.5 and 4 mg., the average being 1.5 mg. The blood of sixteen children with renal conditions was examined. In acute nephritis the nonprotein nitrogenous constituents were found to be within normal limits, and in chronic nephritis they were usually increased.

Leopold and Bernhard arrive at the following conclusions:

1. Figures for the nonprotein nitrogenous constituents of the blood, as well as for the phenolsulphonephthalein excretion of children free from renal disease, are practically identical with the figures obtained from adults, and vary within the normal limits as the adult figures vary.

36. Leopold and Bernhard: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 432.

2. The changes in these figures in children the subjects of renal disease corresponded with the changes observed in adults.

3. The importance of the tests for diagnosis and prognosis, amply demonstrated in adults, will in all probability hold true for children, although a more comprehensive series of cases is required definitely to establish this view.

Tileston and Comfort³⁷ found that the phenolsulphonephthalein excretion for normal children varied between 78 and 81 per cent., while the nonprotein nitrogen of the blood varied between 22 and 26 mg. per 100 c.c. of blood. They investigated three cases of acute nephritis, the phenolsulphonephthalein tests being 39 per cent., 56 per cent. and 54 per cent. The nonprotein nitrogen of the blood in these cases was, respectively, 64, 34 and 24 mg. per 100 c.c. blood. They arrive at the following conclusions:

1. The determination of the total nonprotein nitrogen and urea of the blood is of great assistance in the diagnosis of uremia, and as a guide to the treatment of nephritis, a marked increase in these substances indicating actual or impending uremia, and calling for a diet low in protein. In the diagnosis of nephritis it is inferior to other methods, because many cases of nephritis show no retention of nitrogen.

2. The phenolsulphonephthalein test is very valuable in the diagnosis of nephritis, showing probably better than any other one method the degree of impairment of renal function. In the diagnosis of uremia and as a guide to diet it is inferior to blood analysis, for a low phenolsulphonephthalein output may occur without retention of nitrogen.

3. These investigations of the blood and of the phenolsulphonephthalein excretion would appear to indicate a better secreting capacity of the child's kidney as compared with that of the adult.

Hill³⁸ investigated four different types of tests for kidney function in children.

Phenolsulphonephthalein Test.—In twenty-seven normal children the highest phenolsulphonephthalein test was 100 per cent., the lowest 64 per cent., thus giving an average of 76 per cent. The figures for children are therefore somewhat higher than those for adults. The test was performed on thirty-seven children with nephritis, of all degrees of severity. Twenty-one cases were acute, sixteen chronic. The average excretion of the twenty-one acute cases was 59 per cent., or 17 per cent. below the normal average. The average excretion of the sixteen chronic cases was 63 per cent., or 13 per cent. below the normal average.

37. Tileston and Comfort: AM. JOUR. DIS. CHILD., 1915, 10, 278.

38. Hill: AM. JOUR. DIS. CHILD., 1917, 14, 267.

Added Salt and Urea Test.—This consisted in adding a weighed amount of sodium chlorid and urea to a standard diet, and then determining how much of the added substances could be excreted in twenty-four hours. This test was found to be of little practical value.

"Two-Hour" Renal Test.—The "two-hour" renal test of Hedinger and Schlager was performed in sixteen cases of nephritis and was found to be of considerable value in determining the degree of damage to the kidney. The principle of this test is that a normal kidney can vary the concentration of the urine from hour to hour; a nephritic kidney is likely to lose this ability. This is an extremely delicate test, and very easy to perform; hence it is of considerable practical value.

Blood Urea Nitrogen.—The concentration of blood urea nitrogen was determined in twelve nephritic children and was found to be slightly increased in some, normal in others. In general, the more severe the case appeared clinically, the more retention of urea was there likely to be. This is not a very valuable test for use in children.

The most valuable of the four tests are the phenolsulphonephthalein and the two-hour renal test, and they are valuable not especially in *diagnosis*, but more particularly in *prognosis*.

Zondek³⁹ believes that in considering kidney function it is not correct to look on salt and nitrogen as two separate factors without influence on each other.

Many times we see a kidney which may retain salt and put out nitrogen well, but when we cut down the nitrogen intake the salt excretion improves remarkably. Also, by adding a large amount of nitrogen to the diet, we can diminish the kidney's power of putting out salt. Occasionally we can even make a normal kidney hold back nitrogen by adding an excessive amount of salt to the diet. A salt-free diet is beneficial in reducing blood nitrogen. The question of fluid intake comes in as a third factor, to which a similar rule to the two other factors (sodium chlorid and nitrogen) is attributed. This rule seems to make an exception in the case of Schlager's vascular hyposthenuria during the stage of regeneration of an acute nephritis, where, on account of the decreased power of the kidney to concentrate solids, there is copious diuresis due to the large amount of salt that is being excreted (getting rid of edema), for there is also increased nitrogen output with this increased salt excretion.

The salt concentration of the urine is greater during the daytime, the nitrogen concentration during the night. Normally, Bowman's capsule cares for salt, water and nitrogen excretion. This does not hold, however, for an injured kidney. Damaged kidneys function in an entirely different manner from healthy ones. It is not at all pos-

39. Zondek: Ztschr. f. klin. Med., 1915, 82, 78.

sible to say that any given part of a diseased kidney excretes any given substance or substances. In a damaged kidney, if the damage is particularly to the glomerulus, let us say, the work of excreting salt and nitrogen falls on the tubules, and they might perhaps be able to excrete a fair amount of salt or of nitrogen *alone*, but not of both together. If in feeding a patient with nephritis, little or no salt is given, the tubules can concern themselves with nitrogen excretion alone and do it efficiently.

Zondek has found a diminution in the concentration of nonprotein nitrogen of the blood even when a nephritic child was taking as much as 120 gm. of protein daily, if the diet was salt-free. This is a rather new conception of kidney function, and Zondek in closing his paper makes a special plea for more individualization and less of routine in prescribing the diets of nephritic children.

TREATMENT

Hutinel,⁴⁰ in 1910, summed up in a few words most succinctly the principles to follow in treating nephritis in children. He said:

Let me insist that in dealing with these nephritic children it is especially important to pay attention to careful nursing and hygiene. It is by these measures that the malady is cured, or in the more serious forms, that life is prolonged. Use drugs as little as possible. Especially is it important not to irritate the kidney and to forbid the patient eating any substances whose end-products he cannot eliminate. It is necessary, moreover, to do away with any coexisting infection, however insignificant it may appear, and to watch carefully the mouth, digestive tract, respiratory apparatus, skin, etc. In a word, one must remember that the kidney is delicate, and spare it as far as possible.

This was written seven years ago, but it holds equally well for the principles of treatment today.

Janeway⁴¹ believes that often in dealing with chronic nephritis the protein intake is cut down unnecessarily. He says:

To tell every patient with albuminuria or hypertension to stop eating red meat, or still worse, as I have actually seen done, to go on a milk diet, is evidence either of colossal ignorance or of inexcusable mental laziness. If the phenolsulphonephthalein test is normal I see no reason for restriction of the protein, either qualitatively or quantitatively, below a moderate normal intake.

Epstein⁴² discusses the type of nephritis ordinarily called "chronic parenchymatous," with especial reference to treatment. This is the type of nephritis which is usually associated with the "large white kidney" spoken of in the textbooks, and one of the most striking clinical manifestations of it is the development of edema, which may often

40. Hutinel: Bull. méd., Paris, 1910, **24**, 95.

41. Janeway: Am. Jour. Med. Sc., 1916, **151**, 158.

42. Epstein: Am. Jour. Med. Sc., 1917, **154**, 638.

reach an extreme degree. It is in this condition that the salt-free diet first advocated by Widal and his co-workers has been so successful, and the most generally accepted view of the causation of the edema is that the kidney is unable to excrete salt, and that the water retention is secondary to this. Epstein believes that other factors are perhaps of more importance than salt retention. He has proved that there is a considerable diminution of the protein of the blood serum which is caused by the continuous albuminuria, and that sometimes a nephritic of this type may lose over 20 gm. of protein a day in the urine. As a result of the decrease of protein in the blood serum there is caused a decrease in the osmotic pressure of the blood, which favors the absorption of fluid by the tissues. Therefore, in this particular type of kidney disease, a high and not a low protein diet is indicated. A diet containing a large quantity of protein with a minimum of carbohydrate and fat is the most efficient. The carbohydrate is restricted to promote a maximum assimilation of protein, and to exclude the greater production and retention of water which is incidental in the metabolism of carbohydrates. The fats are excluded because of the marked increase of fatty substances in the blood. The fluid allowed is restricted to the quantity present in the food, plus that which is necessary for the comfort of the individual patient. Enough salt is allowed to make the food palatable.

The diet is made up largely of the following articles: Lean veal, lean ham, whites of eggs, oysters, gelatin, lima beans, lentils, split peas, green peas, mushroom, rice, oatmeal, bananas, skimmed milk, coffee, tea and cocoa.

Christian⁴³ has studied extensively the use of diuretics in nephritis. In most patients with acute nephritis the kidneys will not respond to diuretics and diuretics are likely to do more harm than good. In chronic cases in which edema is of renal origin, diuretic drugs have very little effect in increasing urine output; in the group in which most of the edema is due to cardiac insufficiency, diuretics may work wonders. Theophyllin (theocin) is the best diuretic, but is likely to produce nausea. In nephritis, reduction of fluid intake salt poor diet, sweating and purging are the best methods of removing edema.

Harris⁴⁴ reports several cases of nephritis treated with epinephrin. Ten minims of a 1 to 1,000 solution injected subcutaneously once a day were found to diminish albuminuria and edema. Often a marked diuresis was caused by it.

Ercolani⁴⁵ likewise discusses the use of epinephrin in nephritis. He believes that the adrenals suffer injury in nephritis as well as the

43. Christian: *Dominion med. Monthly*, 1917, **49**, 25.

44. Harris: *Liverpool Med. and Chir. Jour.*, 1916, **36**, 85.

45. Ercolani: *Gazz. d. Osp.*, 1917, **38**, 321.

kidney itself, and that disturbances of the myocardium or of the nervous system in nephritis may be due to a lack of adrenal secretion. According to Ercolani, epinephrin is detoxicating and vasoconstricting in nephritis, both of which processes counteract the infection and ward off injury from the kidneys.

Morse⁴⁶ discusses the Edebohls operation as a therapeutic measure in the nephritis of children and carefully analyzes twenty-three cases in which it was performed. He concludes:

Edebohls' operation is of much value in properly selected cases of nephritis in childhood. It may save life and result in permanent cure in acute nephritis. No child ill with acute nephritis should be allowed to die, therefore, without giving it the advantage of the chance afforded by this operation. It may prolong life for considerable periods in a not inconsiderable number of cases of chronic nephritis, and may possibly, in rare instances, result in cure. It should, therefore, always be considered in all cases of chronic nephritis in childhood which are not responding reasonably well under medical treatment.

99 Commonwealth Avenue.

46. Morse: *Jour. Am. Med. Assn.*, 1917, **69**, 525.

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INTESTINAL INTOXICATION IN INFANTS

THE IMPORTANCE OF IMPAIRED RENAL FUNCTION *

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Preceding the development of toxic symptoms in intestinal intoxication¹ there is pronounced diarrhea, vomiting and diminished ingestion of fluid, the relative importance of which varies in different cases. In the acute stage of the symptoms the excretion of urine is greatly diminished, and at this time the urine contains albumin and abundant casts.

During the past year investigation of cases of intestinal intoxication has furnished evidence which emphasizes the importance of the loss of fluid and the impaired secretion of urine. In this communication it is proposed to present such evidence and to discuss its significance with special reference to the symptomatology.

I. NONPROTEIN NITROGEN AND UREA OF THE BLOOD

*Technic.*²—The nonprotein nitrogen was determined by the method of Gettler and Baker³ except that the final determination was by aeration instead of by distillation. Fiftieth-normal acid and hundredth-normal alkali were used with methyl red as indicator. It was found that the presence of mercury used

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1. It is realized that the use of the term "intestinal intoxication" is open to objections. This term is not applied to the complex described by Finkelstein as "alimentäre intoxicikation" but is used merely to designate the series of toxic symptoms which frequently occur in association with profound nutritional disorders in infants.

The term "diarrhea with toxic symptoms" is cumbersome and is not more exact, for there is not always a direct relation between the severity of the diarrhea and the degree of toxemia. Indeed, there are cases with symptoms indistinguishable from those of intestinal intoxication in which there is no diarrhea at all.

2. All blood for analysis was withdrawn from the superior longitudinal sinus by means of a syringe and the type of needle described in a previous communication. The blood was always taken at least three hours after the last meal.

3. Gettler, A. O., and Baker, W.: Jour. Biol. Chem., 1916, **25**, 211.

in the precipitation of the protein interfered with the aeration of ammonia, probably through the formation of a stable ammonia-mercury compound which was not broken up by alkali. At Dr. Gettler's suggestion potassium hydrogen sulphid was used to precipitate the mercury, and by this means the obstacle was overcome. A very strong pump was used for aeration and blank determinations demonstrated that aeration for one half hour was sufficient. This was shown, (1) by determinations of pure ammonium sulphate or urea, and (2) by distilling mixtures which had been aerated from ten to thirty minutes to determine whether all ammonia had been removed.

As a rule 3 c.c. of blood were used. In some cases in which the nonprotein nitrogen was increased, the determination was made with only 2 c.c. In the earlier cases all determinations were made in duplicate. These were always within the limits of experimental error, and owing to the limited amount of blood one can take from infants, duplicates were omitted in the later cases. The purity of all reagents was checked by blank determinations. Whenever ammonia was present the amount was regularly deducted.

Urea was determined by the urease method of Van Slyke and Cullen.* The enzyme was tested for ureolytic power and also to exclude the presence of ammonia. Fiftieth-normal acid and hundredth-normal alkali were used with methyl red as indicator.

Normal Infants.—Determinations were made on thirty normal infants. Such infants were of practically normal weight, had normal appetite and bowel movements and were apparently well. The values for urea and nonprotein nitrogen are shown in Table 1.

In such infants the nonprotein nitrogen ranged from 23 to 39.1 mg. per 100 c.c. of blood. These figures are considerably higher than those obtained by Minsk and Sauer,⁵ who used Folin's method. The difference is probably due to the difference in methods, as the values for normal adults obtained by Gettler and Baker are higher than those given by Folin's method.

The urea nitrogen was from 4.9 to 14.6 mg. per 100 c.c. of blood. In only a few cases was the urea nitrogen approximately one half of the nonprotein nitrogen, which is generally the case in adults and is what Minsk and Sauer⁵ found in their patients. The difference in these results and those of Minsk and Sauer is due mainly to the fact that the values for nonprotein nitrogen were greater than theirs and not to the difference in the amounts of urea nitrogen.

As shown in Table 1, the amount of urea nitrogen varies greatly in different infants. A careful analysis of the food and the method of feeding fails to reveal an adequate cause for this variation. It seems possible that such variation may be due to the different rate of urea elimination by the kidney in accordance with Ambard's hypothesis.

Infants with Intestinal Intoxication.—Forty-six patients with intestinal intoxication were studied. Thirty-six had acidosis and thirty-three of these showed an increase in the nonprotein nitrogen of the blood. There were, therefore, only three patients with acidosis without

4. Van Slyke, D. D., and Cullen, G. E.: Jour. Am. Med. Assn., 1914 **62**, 1558.

5. Minsk, L. D., and Sauer, L. W.: AM. JOUR. DIS. CHILD., 1917, **12**, 397.

TABLE 1.—THE NONPROTEIN NITROGEN AND UREA NITROGEN IN THE BLOOD OF NORMAL INFANTS *

Number	Age, Months	Weight		Carbon Dioxid Tension Alveolar Air, Mm.	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood
		Lb.	Oz.			
1	1½	9	4	38.2	33.35	8.6
2	1½	9	1	36.6	35.1	7.4
3	1½	9	2	41.2	30.15	13.3
4	2½	10	1	39.1	34.0	12.9
5	2½	10	4	42.4	35.2	10.3
6	3	11	4	40.6	37.6	4.9
7	3½	11	4	37.6	39.1	7.7
8	3½	11	8	35.9	36.2	13.3
9	3½	11	4	38.7	38.0	11.8
10	4	12		41.2	39.1	10.9
11	4½	12	4	40.1	35.2	12.2
12	4½	11	12	36.1	35.4	12.3
13	4½	13	12	40.0	39.0	11.3
14	5½	14	1	39.1	27.6	8.3
15	5½	13	4	36.8	29.3	11.2
16	5½	12	15	40.1	38.2	7.1
17	5½	14	14	44.6	26.6	8.3
18	6	15	3	37.3	27.4	14.6
19	6½	15	14	43.2	34.3	13.9
20	7	18	4	35.3	31.1	7.9
21	7½	17	2	39.2	38.0	11.3
22	7½	16	12	40.3	24.2	11.7
23	7½	17	4	41.2	23.0	7.3
24	8½	17	12	36.7	31.6	10.7
25	9	18		38.9	27.5	4.9
26	9½	18	14	37.6	25.0	10.2
27	10	17	14	42.3	33.4	11.3
28	11	21	11	36.4	34.3	10.1
29	11½	20	4	40.1	31.2	7.2
30	12	21	4	37.5	23.0	9.3

* The air was collected by the Plesch-Higgins method as modified by Howland and Marriott. The air analyses were made in the Haldane apparatus.

an increase of the nonprotein nitrogen. In only one of these patients was more than one determination made. There were four cases without acidosis but with an increased nonprotein nitrogen and four cases with neither acidosis nor increased nonprotein nitrogen. Thirty-seven of the forty-six cases showed a decided increase in the nonprotein nitrogen of the blood.

Twenty-three of the cases with acidosis are shown in Table 2. These were selected for presentation as they were the ones most completely observed, and, moreover, they are representative of the entire series. Of these cases there was only one with no increase in the nonprotein nitrogen (Case 18). In the remainder the nonprotein nitrogen ranged from 57 to 232 mg. per 100 c.c. of blood, the urea nitrogen from 20.1 mg. to 108.2 mg. per 100 c.c. of blood. Comparison with the results from normal infants (Table 1) shows that in intestinal intoxication the urea and nonprotein nitrogen are much increased.

Minsk and Sauer⁵ determined the nonprotein and urea nitrogen in six cases of intestinal intoxication; in three there was a distinct increase. The greatest nonprotein nitrogen in their cases was 67.6 mg. nitrogen per 100 c.c. of blood, which was much lower than in most of my cases. The urea nitrogen in their cases constituted a larger percentage of the nonprotein nitrogen than in my cases, but the actual values for urea nitrogen obtained by them were less.

Discussion.—It is therefore apparent that infants suffering from intestinal intoxication show a marked increase of nonprotein nitrogen and urea in the blood. The nonprotein nitrogen of the blood consists of urea, uric acid, creatin, creatinin, ammonia, amino-acids and probably other substances of unknown nature. As shown in Table 2, the increase in nonprotein nitrogen is due in part only to urea, which comprises less than 50 per cent. of the total nonprotein nitrogen. Determinations of the amounts of uric acid, creatinin, ammonia and amino-acids in this series of cases would have been of interest and perhaps of practical importance, but they were not made, as more blood would have been required than we felt justified in taking. Determinations of these substances, however, have been made in individual cases and are being concluded at the time of preparing this article.

In three cases of the present series uric acid and creatinin were determined and a decided increase found. The results were as follows:

	Nonprotein N, Mg. per 100	Urea N. Mg. per 100	Uric Acid, Mg. per 100	Creatinin, Mg. per 100
Case	C.c. Blood	C.c. Blood	C.c. Blood	C.c. Blood
21	189.0	71.9	18	3.0
22	140.0	59.7	21	2.1
23	159.6	63.2	10	2.9

TABLE 2.—THE NONPROTEIN NITROGEN AND UREA NITROGEN IN THE BLOOD OF INFANTS WITH INTESTINAL INTOXICATION *

Number	Date	Age, Months	Weight		Carbon Dioxid Tension of Alveolar Air, Mm.	C.c. of CO ₂ , Reduced to 0, 760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood
1	1/12	3	Lb.	Oz.	22.0	40.0†	140.0	62.3
	1/14‡		8	15	42.0	92.0	96.0	
	1/18				33.0		29.0	11.1
	1/24					65.0	23.0	
2	1/15	5	10		19.0		58.0	20.1
	1/16				20.0	86.0	123.0	
3	2/ 2	5½	12	4	14.7§	26.0	140.0	
	2/ 5				17.4§		198.2	
	2/ 6					34.0	184.3	
4	3/ 2	4	6	6	31.87§		137.0	
	3/ 3				21.0	42.0	193.0	
5	3/ 5	3	8	8	17.0		150.0	84.0
	3/ 6					38.0	109.0	75.6
6	3/10	5½	5	9	34.2§		83.0	39.0
	3/12					40.0	73.0	
	3/13				22.0		97.0	
7	3/19	4	13	6	35.1§		78.6	25.2
	3/20				17.2§			
	3/21					88.0		
	3/26‡				36.4§	100.0	57.0	15.9
8	4/13	9	17		28.4§		142.0	72.1
	4/19‡				56.0	97.0	127.0	64.3
	4/26					69.0	95.0	
9		6	11	4	21.5§	40.0	84.0	39.7
10		11½	12		17.0		61.9	
11		13	15	3	23.4§	25.1	124.0	44.8
12		6	12	8	25.0		133.0	39.1
13	5/16	5	11	12	23.0		134.4	
	5/17‡				37.5§	76.0	176.9	76.58
14		8½	14	3	17.0		232.0	106.2
15		5	10	4	23.6§		179.0	66.4
16		7	13	1	26.1§		58.8	27.6
17		8½	14	2	16.0	34.0	143.0	73.7
18		9½	13	4	16.0		36.0	13.2
19	11/11	7	11	6	21.3§		176.0	89.0
	11/18‡				38.0		160.0	
	11/24						28.0	7.0
20	5/20	9	14	8	14.4§	23.2	211.0	96.1
	5/25‡				44.3§		50.1	13.4
21	5/23	9	14	4	24.6§		139.0	71.9
	5/27‡				39.6§		34.0	14.0
22	6/ 1	10	15	6	23.0		140.0	59.7
23		13	19		25.0		159.6	63.2

* This table includes only part of the cases, as forty-four cases of intestinal intoxication were investigated. The results were so uniform that it seemed superfluous to tabulate all cases. Some of the additional cases will be cited in the text.

† These values are cited merely in general confirmation of the alveolar air analyses. They cannot be compared accurately with the figures for alveolar air, since the values for the carbon dioxid of alveolar air represent venous blood while the plasma analyses are probably more nearly representative of arterial blood. In a late series of cases, to be reported shortly, this discrepancy has been eliminated.

‡ After treatment. The treatment comprised the administration of 2 to 7 gm. of sodium bicarbonate by subcutaneous or intravenous injection and giving large amounts of water by mouth, or salt solution subcutaneously or intravenously.

§ Air collected by the method of Fiesch-Higgins as adapted to infants by Howland and Marriott and analyzed in the Haldane apparatus. The remaining figures represent alveolar air collected in the same way but determined by the colorimetric method of Marriott.

TABLE 3.—THE CORPUSCULAR VOLUME AND TOTAL SOLIDS OF THE BLOOD; THE SPECIFIC GRAVITY AND TOTAL NITROGEN OF THE BLOOD SERUM OF NORMAL INFANTS *

Number	Total Solids of the Blood, per Cent.	Corpuscular Volume of the Blood, per Cent.	Specific Gravity of the Blood Serum	Total Nitrogen of the Blood Serum, Gm. per 100 C.c.	Ratio of Nonprotein Nitrogen of Blood to Total Nitrogen of the Blood Serum N.P.N. : T.N.
1		35.2	1.021	1.123	1 : 34
2		34.3	1.023	1.098	1 : 31
3		33.9	1.024	1.101	1 : 37
4		42.0	1.023	0.9876	1 : 29
5		38.0	1.021	1.043	1 : 30
6		32.5	1.020	1.131	1 : 32
7		35.5	1.022	1.198	1 : 31
8		34.0	1.020	1.11	1 : 31
9		33.0	1.025	1.02	1 : 27
10		29.0	1.024	0.983	1 : 25
11		34.0	1.025	1.13	1 : 32
12		31.0	1.023	0.987	1 : 28
13	18.6	45.0	1.022	1.061	1 : 27
14	17.9	39.0	1.020	1.113	1 : 40
15		32.0	1.021	0.997	1 : 33
16	17.5	33.0	1.023	1.043	1 : 28
17	17.1	29.8	1.024	1.121	1 : 41
18		32.0	1.023	1.099	1 : 40
19	17.7	36.0	1.020	1.00	1 : 29
20		37.0	1.023	0.988	1 : 32
21		33.0	1.025	1.13	1 : 31
22	18.4	33.0	1.020	1.108	1 : 46
23	17.3	31.0	1.024	1.16	1 : 50
24	18.2	39.0	1.023	0.977	1 : 30
25	17.2	32.9	1.021	1.111	1 : 40
26		34.0	1.020	1.023	1 : 41
27		32.0	1.021	1.101	1 : 29
28	17.4	34.0	1.022	1.097	1 : 32
29		35.0	1.023	1.114	1 : 36
30	18.5	39.3	1.025	1.01	1 : 36

* The figures in this table were obtained from the same infants as those in Table 1 and are numbered the same. To avoid needless repetition the age, weight, etc., are not given in the foregoing table as they are shown in Table 1.

The substances comprising the nonprotein nitrogen are normally excreted in the urine, and an accumulation in the blood usually signifies an impairment of renal function. While this interpretation is generally accepted, yet in connection with infantile diarrhea another possibility must be considered. The loss of water through the bowels in diarrhea is one of the most prominent clinical features of the disease and the question naturally arises whether this loss of water could be responsible for the high nonprotein nitrogen in the blood. If the blood became more concentrated through loss of water, it seems possible that there could be a relative increase of nonprotein nitrogen due to this cause. Such an increase, however, would be merely apparent.

To obtain evidence bearing on this possibility, determinations of the blood concentration were made.

II. THE CONCENTRATION OF THE BLOOD

1. *Corpuscular Volume*.—This was determined in the special pipet of Gettler and Baker⁴ and in the manner described by them.

The corpuscular volume of normal infants ranges from 31 to 42 volumes per cent. (Table 3). Gettler and Baker found in normal adults that the corpuscular volume ranged from 33 to 50 volumes per cent., which values are considerably higher than those in normal infants.

In cases of intestinal intoxication the values were from 32 to 49 volumes per cent. (Table 4). Comparison of Tables 3 and 4 shows that in cases of intestinal intoxication the average corpuscular volume is higher, and in a number of the individual cases this increase is marked. The corpuscular volume, however, is not regularly increased in the cases of intoxication, and in a number of instances, despite the increase in nonprotein nitrogen, the corpuscular volume was within normal limits. Of most significance was the fact that there was no direct ratio between the corpuscular volume and the nonprotein nitrogen. For example, Case 5 showed a corpuscular volume of 38 and a nonprotein nitrogen of 150 mg. per 100 c.c. of blood, and later a corpuscular volume of 30 and a nonprotein nitrogen of 169. In both instances the corpuscular volume is within normal limits while the nonprotein nitrogen is greatly increased. Moreover, the second determination showed a lower corpuscular volume in the presence of a slightly increased nonprotein nitrogen. The same evidence is shown in several of the tabulated cases.

These determinations show that there is no constant decrease of the blood plasma in relation to corpuscles and that according to these results the high nonprotein nitrogen in cases of intestinal intoxication cannot be explained on the basis of increased blood concentration.

This argument would be valid only if, in intestinal intoxication, there was no increased destruction of red cells and if the red cells were

TABLE 4.—THE CORPUSCULAR VOLUME AND TOTAL SOLIDS OF THE BLOOD; THE SPECIFIC GRAVITY AND TOTAL NITROGEN OF THE BLOOD SERUM OF INFANTS WITH INTESTINAL INTOXICATION *

Number	Date	Total Solids of the Blood, per Cent.	Corpuscular Volume of the Blood, per Cent.	Specific Gravity of the Blood Serum	Total Nitrogen of the Blood Serum, Gm. per 100 C.c.	Ratio of the Nonprotein Nitrogen of the Blood to the Total Nitrogen of the Blood Serum N.P.N : T.N.
1	1/12		86.0	1.0279	1.397	1 : 10
	1/14		87.0	1.025	1.36	1 : 14
	1/18		82.0	1.023	1.11	1 : 33†
2	1/15		89.5	1.026	—	
	1/16	21.8	—	1.027	1.55	1 : 13
3	2/ 2		47.0	1.029	1.36	1 : 10
	2/ 6	20.4	84.0	1.029	1.219	1 : 6
4	3/ 2		82.0	—	—	
	3/ 8	20.9	81.0	1.030	1.368	1 : 7
5	3/ 5	20.6	88.0	1.031	—	
	3/ 6	19.7	80.0	1.027	1.112	1 : 7
6	3/10	21.1	—	1.028	1.114	1 : 13
	3/12	20.0	—	—	0.914	1 : 12
	3/13		87.0	1.030	1.28	1 : 13
7	3/19		49.0	1.030	1.176	1 : 15
	3/21		89.0	—	—	
	3/26	20.8	85.0	1.024	0.986	1 : 17
8	4/18	21.6	87.0	1.032	1.513	1 : 11
	4/19	21.1	42.0	1.030	1.42	1 : 11
	4/26	19.3	27.0	1.023	0.942	1 : 10
9			—	—	—	
10			85.0	1.024	1.067	1 : 17
11			89.0	1.030	—	
12		20.8	49.0	1.023	1.213	1 : 9
13	5/16	21.3	42.0	1.029	1.368	1 : 10
	5/17		87.0	1.026	1.204	1 : 7
14		21.1	49.0		1.36	1 : 6
15				1.030	1.302	1 : 7
16		17.4		1.023	0.980	1 : 17
17			47.0	1.029		
18			29.0	1.026		
19	11/11	19.9	89.6	1.030	1.3	1 : 7
	11/18		88.4		1.23	1 : 8
	11/24	18.9†	84.0	1.027	1.09	1 : 33†
20	5/20	21.7	39.8	1.031	1.365	1 : 6
	5/25	19.1†	87.0	1.025	1.071	1 : 22†
21	5/23	21.6	45.0	1.029	1.361	1 : 7
	5/27	18.5†	88.9	1.023	1.14	1 : 33†
22	..		49.9	1.030	1.293	1 : 9
23			46.2	1.031	1.321	1 : 8

* The figures in this table were obtained from the same infants as those in Table 2 and are numbered the same. To avoid needless repetition the age, weight, etc., are not given in the above table as they are in Table 2. See footnotes * and † Table 2.

† After treatment.

of normal size. Obviously, a marked destruction of red cells would decrease the corpuscular volume while an increase or decrease in the size of the cells would be of marked influence. Whether there is an increased blood destruction in intestinal intoxication is impossible to say, but there is no evidence to support such a view. Fresh blood preparations have been examined in a number of cases and these showed no apparent change in the size of the red cells.

2. Specific Gravity of the Blood Serum.—The specific gravity was determined by weighing the blood serum in small Nicholl pyknometers with a capacity of from 0.4 to 1.5 gm. of water. All determinations were at 22° C.

The specific gravity of the blood serum of normal infants varies from 1.020 to 1.025 (Table 3). These values are lower than those in normal adults, which, according to Gettler and Baker,³ are from 1.026 to 1.030. In cases of intoxication the specific gravity was from 1.026 to 1.031, which is greater than that of normal infants. This increase, however, is too slight to account for the increase in nonprotein nitrogen merely on the basis of increased blood concentration.

Assuming that the normal specific gravity of the blood serum of infants is 1.020, this signifies that each 100 c.c. of blood serum contains 2 gm. of dissolved solids. An increase of the specific gravity to 1.031, which was the maximum found in cases of intoxication, would indicate an increase of 1.1 gm. of solids per 100 c.c. This would merely signify that the serum contained a trifle more than one and one-half times as much solids as normal. In the cases of intestinal intoxication, we find that the nonprotein nitrogen is often five times as great as normal, and if this increase were merely a matter of increased blood concentration, all solids should be equally affected and the specific gravity should be as great as 1.100. In no instance was the specific gravity increased to any degree comparable to the increase in nonprotein nitrogen. Moreover, a comparison of the nonprotein nitrogen and specific gravity in cases of intoxication shows that there is no direct ratio and that in several instances there was a great increase in the nonprotein nitrogen, with a specific gravity within the limits of normal. Moreover, the mere increase in nonprotein nitrogen would cause an increase in the specific gravity of the serum aside from any increase in concentration due to loss of fluid from the blood.

3. Total Nitrogen of the Blood Serum.—One half to 1 c.c. of blood serum was digested in a small Kjeldahl flask with 2 c.c. of sulphuric acid, about 0.5 gm. of potassium sulphate and a small crystal of copper sulphate. The determination was made by aeration into twentieth-normal acid and titration with twentieth-normal sodium hydroxid, using congo red as indicator.

If the increase of nonprotein nitrogen in the blood of infants suffering from intestinal intoxication is due merely to increased concentra-

tion of the blood, there should be a similar increase in the other substances comprising the total nitrogen of the blood. That such is not the case is readily seen by referring to Tables 3 and 4.⁶ While there is a greater total nitrogen of the blood serum in cases of intoxication, this increase is in no way comparable to the increase of nonprotein nitrogen, and in several cases the increase in total nitrogen can be explained almost entirely by the increase in nonprotein nitrogen. This is shown best by comparing the nonprotein nitrogen:total nitrogen ratio in the normal cases with those of intoxication.

4. *Total Solids of the Blood.*—The total solids were determined by weighing a few drops of blood on blotting paper previously weighed, drying at 110 C. and again weighing.

As shown in Table 3, the total solids in normal infants ranged from 17.1 to 18.6 per cent. In cases of intoxication (Table 4) the values were from 19.6 to 21.8 per cent. These figures agree closely with those recently published by Courtney and Fales⁷ and have the same significance as those for corpuscular volume, total nitrogen and specific gravity.

TABLE 5.—SHOWING THE RETENTION OF NONPROTEIN NITROGEN AND UREA AFTER THE BLOOD CONCENTRATION BECAME NORMAL

Date	Weight, Pounds	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood	Specific Gravity of Blood Serum	Total Nitrogen in Blood Serum, Gm. per 100 C.c.	Corpuscular Volume, per Cent.
11/11	11½	176	89	1.080	1.801	89.6
11/18	11	160	..		1.23	88.4
11/20	11½	120	50	1.028	1.18	84.5
11/22	11½	100	..	1.025	1.12	
11/24	11½	28	7	1.024	1.09	84.0

Baby G. (Case 19) was admitted Nov. 11, 1916, with a history of severe diarrhea and vomiting for four days. The infant was greatly emaciated and the fontanel was sunken. The mental condition was dull. Hyperpnea was marked and the carbon dioxide tension of the alveolar air was 19 mm.

Seven and a half grams of sodium bicarbonate were given by intravenous injection. The carbon dioxide tension of the alveolar air became normal and the hyperpnea ceased. Large amounts of water were given by mouth and by subcutaneous injection (physiologic sodium chloride solution).

Discussion.—It is of interest that the corpuscular volume of the blood, the total solids of the blood, the total nitrogen and specific gravity of the blood serum are all much lower in normal infants than in

6. In adults Gettler and Baker (Footnote 3) found that the total nitrogen of the blood serum was from 1.2 to 1.4 gm. per 100 c.c. These values are much greater than those from normal infants.

7. Courtney, A. M., and Fales, H. L.: AM. JOUR. DIS. CHILD., 1917, 14, 202.

adults. This is probably in correspondence with the fact that the tissues of the infant contain a higher percentage of water and that the water metabolism is more active in infants than in adults.

The data furnished by the total nitrogen, specific gravity, corpuscular volume and total solids indicate that in intestinal intoxication there is often an increase in blood concentration. This increase in concentration, however, is insufficient to account for the increase in nonprotein nitrogen found in these cases.

Further evidence bearing on this question is the observation that a number of patients begin to retain fluid for some time before the non-protein nitrogen falls to normal. The nonprotein nitrogen remains high after the corpuscular volume of the blood and total nitrogen and specific gravity of the serum reach normal. This would indicate that the high nonprotein nitrogen was not due merely to the increased blood concentration. The results from a case of this kind are shown in Table 5.

On the basis of the evidence given it seems that the increased non-protein nitrogen which occurs in cases of intestinal intoxication is due to defective elimination of the nitrogenous waste products by the kidney.

III. TESTS OF RENAL FUNCTION. PHENOLSULPHONEPHTHALEIN ELIMINATION: AMBARD'S COEFFICIENT OF UREA EXCRETION

Phenolsulphonephthalein Elimination: Technic.—The infant was put on a metabolism frame three hours after the last feeding and was given 120 c.c. of slightly sweetened water. Three mg. of phenolsulphonephthalein were given intramuscularly and the urine collected for two hours. One half of the urine was used to determine the phthalein in a Rowntree and Geraghty modification of the Autenreith-Königsberger colorimeter; the other half was used for estimation of urea, ammonia and total nitrogen.

Tests were made on thirty normal infants from 3 months to 1 year of age. The phenolsulphonephthalein elimination ranged from 58 to 94 per cent. during two hours, the water elimination from 56 to 100 c.c. (47.5 to 83.5 per cent.). (Table 6.)

The results from 16 infants with intoxication are shown in Table 7. The phenolsulphonephthalein elimination was from 4 to 38 per cent., the water elimination from 23 to 48 c.c. (19 to 40 per cent.). The interpretation of these results in terms of renal permeability cannot be made with any degree of assurance, owing to the greatly diminished secretion of urine. During the acute stage of intestinal intoxication the infant may pass no urine for hours and the twenty-four hour elimination may total only a few cubic centimeters. For this reason, in the cases of intestinal intoxication used for the phenolsulphonephthalein test the patients had recovered from the acute stage and had commenced

TABLE 6.—THE ELIMINATION OF WATER AND PHENOLSULPHONEPHTHALEIN; AMBARD'S COEFFICIENT OF UREA EXCRETION. NORMAL INFANTS

Number	Age, Months	Weight, Pounds	Water Elimination after Ingestion of 120 C.c. of Water, 2 Hour Period		Phenol- sulphone- phthalein Output, 2 Hour Period, per Cent.	Ambard's Coefficient of Urea Excretion, 2 Hour Period, Ur $\checkmark D \frac{\sqrt{c}}{\sqrt{5}}$
			O.c.	per Cent.		
1	8	11½	66	55.0	80	0.072
2	8½	10½	80	67.5	64	0.061
3	4	12½	90	75.0	68	0.066
4	4	11½	58	47.5	96	0.064
5	5	18	74	61.5	58	0.10
6	5½	18½	94	78.0	78	0.071
7	6	14½	59	49.0	67	0.05
8	6	15	67	56.0	74	0.11
9	6½	14½	66	71.5	88	0.065
10	7	16½	78	61.0	71	0.068
11	7	16	81	62.5	81	0.061
12	7½	15½	59	49.0	61	0.01
13	8	16½	62	52.0	70	0.072
14	8	17½	56	47.5	59	0.076
15	10½	18	79	66.0	86	0.068
16	11	19½	100	83.5	94	0.05
17	12	20½	77	64.0	87	0.078
18	13	21	67	56.0	75	0.087
19	13	20½	99	82.5	71	0.061
20	13½	21½	78	66.0	78	0.072

to pass moderate amounts of urine. No test was included during which less than 20 c.c. of urine was voided. Despite the selection of cases and the fact that 120 c.c. of water were ingested at the time of the test, the water output was greatly diminished. As shown by Tables 6 and 7, the phenolsulphonephthalein elimination was greatly diminished in cases of intoxication. Owing to the decreased secretion of urine the low phenolsulphonephthalein output cannot be attributed to an anatomic kidney lesion.

Ambard's Coefficient of Urea Excretion.—According to Ambard⁸

8. Ambard, L.: *Physiologie normale et pathologique des reins*, Paris, 1914; Ambard, L., and Weill, A.: *Jour. de physiol. et de pathol. gén.*, 1912, **32**, 217. This subject has also been considered in detail by McLean, F. C., and Selling, L.: *Jour. Biol. Chem.*, 1914, **19**, 31; McLean, F. C.: *Jour. Exper. Med.*, 1915, **22**, 212; Addis, T., and Watanabe, C. K.: *Jour. Biol. Chem.*, 1916, **24**, 203, and Lewis, D. S.: *Arch. Int. Med.*, 1917, **19**, 1.

TABLE 7.—THE ELIMINATION OF WATER AND PHENOLSULPHONEPHTHALEIN;
AMBARD'S COEFFICIENT OF UREA EXCRETION. INFANTS,
WITH INTESTINAL INTOXICATION *

Number	Age, Months	Weight, Pounds	Water Elimination after Ingestion of 120 C.c. of Water, 2 Hour Period		Phenol- sulphone- phthalein Output, 2 Hour Period, per Cent.	Ambard's Coefficient of Urea Excretion, 2 Hour Period, Ur $\checkmark D \frac{\sqrt{C}}{\sqrt{P}}$
			C.c.	per Cent.		
1	8	8%	26	13.0	22.0	0.23
2	4½	9%	31	26.0	18.0	0.31
3	5	9	40	33.0	29.0	0.21
4	5½	10	25	31.0	34.0	0.19
5	6½	9%	48	40.0	34.0	0.22
6	7½	12½	35	29.0	17.0	0.36
7	7½	11%	29	24.0	20.0	0.27
8	8	13½	31	26.0	23.0	0.29
9	8½	12%	23	15.0	15.5	0.27
10	9	14	47	40.0	38.0	0.10
11	9	13½	36	30.0	27.0	0.17
12	10½	12%	28	23.0	14.0	0.37
13	10%	13%	30	25.0	30.0	0.20
14	11	14	37	31.0	29.0	0.27
15	11½	13%	44	37.0	39.0	0.18
16	11%	15½	33	27.5	20.0	0.28

* During the acute stage of intestinal intoxication so little urine is secreted that tests of renal function are impossible. The figures shown were derived from a study of patients who had begun to improve and who excreted more than 20 c.c. of urine during the two-hour period.

and his co-workers there is a definite ratio between the urea in the circulating blood and that excreted in the urine per unit of time. The formula used to derive the coefficient is obtained from Ambard's third law and is as follows:

$$K = \frac{Ur}{\sqrt{D \frac{70}{P} \frac{\sqrt{C}}{\sqrt{25}}}}$$

K=Coefficient of urea excretion.

Ur=Urea per liter of blood.

D=Output of urea for twenty-four hours calculated from the amount excreted during the period of observation.

P=Weight of patient in kilograms.

C=Grams of urea per liter of urine.

70=Standard weight.

25=Normal amount of urea per liter of urine.

Our observations were made during two-hour periods at the same time the phenolsulphonephthalein tests were made. The analytical methods were those previously described.

In applying Ambard's formula to infants it is obvious that certain changes must be made. In the formula the standard weight of 70 kg. is used. This is, of course, relative to adults. It is practically impossible to introduce a standard weight for young infants owing to the fact that the weight changes are so rapid. The use of the average weights for different ages would not be strictly accurate, since the weights of normal infants of the same ages may vary within several pounds, which makes a considerable error when one considers such differences in relation to total weight. A further difficulty arises from the circumstance that infants with nutritional disorders show great fluctuations in weight within short periods of time. Actual calculations in normal cases show that the coefficient is more constant if the factor 70/P or any equivalent is eliminated.

For adults the standard value of 25 gm. of urea per liter of urine is used. Our determinations on thirty normal infants under 1 year of age gave figures which ranged from 4.2 to 6.37 gm. of urea per liter. On the basis of these figures the standard value of 5 was substituted for 25 in the formula. As used by us the formula was as follows:

$$K = \frac{Ur}{\sqrt{D \frac{\sqrt{C}}{\sqrt{5}}}}$$

In adults it has been found that the normal coefficient ranges from 0.6 to 0.9 and that defective kidney function causes the constant to increase. In normal infants the constant, as calculated by the formula we used, ranges from 0.05 to 0.11 (Table 6). The coefficient, therefore, has a tendency to be higher in infants than in adults, and in several of our normal cases values above 0.09 were obtained which in adults would signify impairment of renal function.

In cases of intoxication the constant ranged from 0.13 to 0.39, thus indicating a considerable degree of impairment of renal function (Table 7).

In general, these results are roughly parallel to the phenolsulphonephthalein elimination and are open to the same criticism in reference to the excretion of water. All that these tests signify is that in intestinal intoxication the power of elimination by the urine is greatly impaired.

IV. THE CAUSE OF DEFICIENT ELIMINATION BY THE KIDNEYS

In consideration of the greatly diminished excretion of urine during the acute stage of intestinal intoxication it seems only natural to expect that substances normally excreted in the urine would be retained. This would certainly occur unless there were some other channel through which the waste products could be eliminated. Despite the self evidence of this proposition it is a question of some importance whether the retention is entirely a matter of lessened water excretion, or whether it is dependent on a kidney lesion.

The occurrence of albumin and casts in the urine of infants affected with severe diarrhea has long been recognized and is mentioned in practically every treatise on this disease. The subject was considered in detail by Pick,⁹ in 1905, who gave an exhaustive review of the literature. He noted that the toxic symptoms in severe diarrhea are not unlike those of uremia, and suggested the possibility that in some cases the symptoms may be of uremic origin.

Neuman,¹⁰ in 1907, found that in general there was a close parallel between the presence and degree of albuminuria and cylindruria and the severity of the toxic symptoms. He concluded, however, that the renal lesions were probably secondary and not of etiologic importance.

In all of the cases in this series the urine contained albumin and casts during the acute stage of the disease. With improvement in the symptoms, albumin and casts soon disappeared. The degree of albuminuria, however, was rarely great and not often of sufficient amount to give a reading in the Esbach tube. In most instances the number of casts seemed much greater than one would expect from the amount of albumin present. The period at which the albuminuria and cylindruria were most marked coincided with the period when the urine was very scanty, so that the number of casts, at least, would appear much greater than it actually was.

A detailed consideration of the significance of albumin and casts in the urine is beyond the scope of this paper. Certainly their presence is abnormal, but whether their occurrence indicates a kidney lesion capable of causing retention of nitrogenous waste products is impossible to determine. It does seem clearly established, however, that the occurrence of albuminuria and cylindruria does not necessarily indicate a kidney lesion which is demonstrable by our present histologic methods. If definite anatomic lesions are the sole criteria of kidney disease, we should not be warranted in assuming that a kidney lesion was present solely on the basis of albuminuria and cylindruria.

9. Pick, J.: Arch. f. Kinderh., 1905, **40**, 291.

10. Neuman, G.: Jahrb. f. Kinderh., 1907, **66**, 633.

Neuman¹⁰ found slight parenchymatous renal lesions in one of his cases. In another, the kidneys were practically normal. Pick,⁹ however, found distinct anatomic lesions in several cases. Definite renal lesions in infants dying of intestinal intoxication were described by Hoffsten,¹¹ Epstein,¹² Bernhard and Felsenthal,¹³ Czerny and Moser,¹⁴ Jehle¹⁵ and others.

In nine of the cases presented in this paper necropsies were performed and the results are shown in Table 8. In two cases, 14 and H., there was distinct parenchymatous nephritis, severe in one (14) and moderate in the other (H.). In both of these cases the tubules contained many necrotic cells which were often massed to form distinct foci. These foci stained a deep blue with hematoxylin, which suggested the deposition of calcium salts. The lesions in these cases resembled closely those seen in poisoning with mercuric chlorid. Three cases, 10, 5 and O'D., showed no definite renal changes at all. The remaining four cases showed slight or moderate parenchymatous changes in the tubular epithelium and hemorrhage into the tubules. Dr. Charles Norris, who kindly examined the sections, stated that the hemorrhage was possibly agonal and in consequence may have borne no direct relation to the disease. This is suggested strongly by the fact that the urine of none of these patients contained blood, which should have been true had the hemorrhage existed for some time before death.

Unfortunately, there is no evidence available which indicates the degree of kidney damage necessary to cause retention. On the basis, however, of the lesions present in nephritis in adults with nonprotein nitrogen retention it would seem that in only two of our cases was the kidney lesion sufficient to account for the high nonprotein nitrogen. Lesions of similar grade to those found in the other cases are often found in the absence of any chemical evidence of defective renal function.

It seems apparent, therefore, that the impairment of renal function in intestinal intoxication cannot be due in the majority of cases to a definite kidney lesion, but must depend on some other cause. It seems most probable that the cause lies in the depleted water supply of the body.

It is well established that water is the most efficient diuretic, and without an adequate supply secretion of urine is impossible. In intestinal intoxication the water supply of the body is usually depleted by the great loss of water in the stools. Many of the patients refuse to

11. Hoffsten: *Virchow-Hirsch Jahresb.*, 1888, **11**, 478.

12. Epstein: *Festschrift Edw. Henoch*, Berlin, 1890.

13. Bernhard and Felsenthal: *Arch. f. Kinderh.*, 1894, **17**, 222.

14. Czerny and Moser: *Jahrb. f. Kinderh.*, 1894, **38**, 430.

15. Jehle: *Jahrb. f. Kinderh.*, 1907, **65**, 40, Part 1.

TABLE 8.—EVIDENCES OF RENAL INVOLVEMENT IN NINE CASES OF INTESTINAL INTOXICATION

Patient	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Albumin in Urine	Casts in Urine	Evidence of Renal Lesions	
				Macroscopic	Microscopic
10*	61.9	+ Trace	Few hyaline many granular	Moderate congestion; no swelling of cortex; markings distinct	No significant lesions
13*	134.4	Heavy trace	Many hyaline granular and epithelial	Cortex pale, slightly swollen; markings slightly obscured	Many tubules contain red blood cells; tubular epithelium shows parenchymatous degeneration; apparent increase in nuclei in malpighian corpuscles, possibly due to shrinkage
14*	232.0	1 Gm. per liter by Esbach	Many granular and epithelial	Kidneys pale; greatly enlarged; edematous; cortex much swollen and markings obscured	Marked swelling and necrosis of tubular epithelium; foci of necrotic cells in tubules of cortex; coagulated material in glomeruli; apparent increase in number of cells in malpighian tufts; definite acute parenchymatous nephritis
6*	88.0	Trace	Many hyaline few granular	Kidneys slightly enlarged; cortex slightly swollen	Moderate swelling and parenchymatous degeneration of tubular epithelium; nuclei slightly pale
5*	150.0	Trace	Many hyaline few granular	Slight congestion	No significant lesions
P	113.4	Trace	Few hyaline many granular	Kidneys pale; slightly enlarged; cortex slightly swollen; slight edema	Many tubules contain red blood cells; parenchymatous degeneration of tubular epithelium
H	65.8	Moderate 1.5 Gm. per liter by Esbach	Many hyaline and granular	Kidneys pale; slight swelling of cortex	Marked hemorrhage into tubules of pyramids; hemorrhage into glomeruli; necrosis of tubular epithelium with the formation of a few necrotic foci in tubules; acute parenchymatous nephritis
V	90.3	Trace	Many hyaline few granular	Slight enlargement of kidneys; marked congestion	Hemorrhage into tubules; tubular epithelium shows moderate parenchymatous degeneration
O'D	68.0	Trace	Many hyaline few granular	Slight congestion	No significant lesions

* These figures refer to the same patients as those in Tables 2 and 4.

† A few red blood cells in urine.

ingest even water and vomit water or food, so that there is but little fluid available to replace even the normal loss of water in the excretions. It seems probable, therefore, that the deficient elimination by the kidney is purely functional and is due to the fact that there is no water available for the formation of urine.

The fact that the increased concentration of the blood is insufficient to account for the high nonprotein nitrogen is in no way antagonistic to this idea. There are a number of factors which tend to keep normal the water composition of the blood.

Bang¹⁶ found that when dogs are deprived of water the blood shows increased nonprotein nitrogen. The nonprotein nitrogen became normal when water was given in sufficient amounts. Bang gave no evidence bearing on the blood concentration. It seems quite possible that the high nonprotein nitrogen was due to defective elimination owing to lack of water.

The clinical importance of the great loss of water in intestinal intoxication is too well known to require special consideration. It is a matter of considerable difficulty to give these infants sufficient water to replace that lost in the excretions. In six cases of intoxication in which it was possible to give sufficient water approximately to replace that lost the excretion of urine was apparently normal and there was no significant increase in the nonprotein nitrogen of the blood. Of the same significance is the fact that in no case was there any material reduction in the nonprotein nitrogen of the blood before the normal excretion of urine was reestablished.

From the evidence at our disposal it seems probable that the deficient kidney elimination in intestinal intoxication is dependent, to a great degree at least, on the negative water balance. Whether insufficient water in the blood and tissues is directly and entirely responsible for the diminished secretion of urine offers considerable field for discussion. There are a number of factors capable of affecting kidney function which may be of influence. It has been demonstrated by Starling¹⁷ that the colloids of normal blood exert an osmotic pressure of 25 to 30 mm. of mercury and under these conditions the arterial pressure in the kidney glomeruli must be greater than 30 mm. of mercury to insure the formation of urine. A greater concentration of colloids would require a greater arterial pressure in the kidney for glomerular filtration to occur.

In intestinal intoxication it seems possible that the blood colloids may be increased to such degree that they exert an osmotic pressure greater than the pressure in the glomerular capillaries. If this were

16. Bang, I.: *Biochem. Ztschr.*, 1915, **72**, 119.

17. Starling: *Jour. Physiol.*, 1899, **24**, 317.

true the formation of urine would be prevented. Moreover, the total blood volume is probably reduced in cases of intestinal intoxication, which would diminish the blood flow through the kidney and consequently reduce the secretion of urine. Such conditions, however, would arise in great part, if not entirely, from the water deficit and at present have not been accurately determined.¹⁸

V. THE ACIDOSIS OF INTESTINAL INTOXICATION

Howland and Marriott¹⁹ showed that acidosis is a frequent occurrence in severe diarrhea in infants. The frequency and degree of acidosis in cases of intestinal intoxication has been discussed also by Schloss and Stetson.²⁰

According to our present conception, acidosis is best defined as a reduction in the alkaline reserve of the blood. Our knowledge of the significance of the alkaline reserve and the factors which influence it is based on the work of Henderson²¹ and Henderson and Palmer,²² and has been discussed by Lundsgaard,²³ Peabody,²⁴ Hasselbalch and Gammeltoft,²⁵ Barcroft,²⁶ Howland and Marriott,²⁷ Van Slyke and Cullen²⁸ and others.

On the basis of this definition it is theoretically possible for acidosis to be due to several causes. In acidosis occurring with diarrhea Howland and Marriott¹⁹ found no evidence that abnormal acids were formed. They found no significant increase in the acetone bodies in the blood, which demonstrated that the acidosis was not due to increased formation or diminished oxidation of these substances.

18. There is no means of ascertaining the blood pressure in the kidney of human beings. In dogs it is assumed to be 20 per cent. less than the carotid blood pressure, but Cushny states that such assumption is little more than a guess (*The Secretion of Urine*, London, 1917). MacKenzie (*Brit. Jour. Child. Dis.*, 1912, **9**, 343) says that the anuria in severe diarrhea of infants is due to lowered blood pressure, although he gives no evidence to support this view. Hill (*Arch. Pediat.*, 1913, **30**, 588) has reported blood pressure determinations (femoral artery) in eighteen cases of severe diarrhea. His results show no reduction in blood pressure when compared with the values for normal infants obtained by Morse and Wyman (*AM. JOUR. DIS. CHILD.*, 1914, **8**, 270) and others.

19. Howland, J., and Marriott, W. McK.: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 309.

20. Schloss, O. M., and Stetson, R. E.: *AM. JOUR. DIS. CHILD.*, 1917, **13**, 218.

21. Henderson, L. J.: *Am. Jour. Physiol.*, 1908, **21**, 427; *Ergebn. d. Physiol.*, 1909, **8**, 254; *Jour. Biol. Chem.*, 1911, **9**, 403.

22. Henderson, L. J., and Palmer, W. W.: *Jour. Biol. Chem.*, 1912-1913, **8**, 393; 1913, **14**, 81; 1914, **17**, 305.

23. Lundsgaard, C.: *Biochem. Ztschr.*, 1912, **41**, 149.

24. Peabody, F. W.: *Arch. Int. Med.*, 1914, **14**, 236.

25. Hasselbalch, K. A., and Gammeltoft, S. A.: *Biochem. Ztschr.*, 1915, p. 205.

26. Barcroft, J.: *The Respiratory Function of the Blood*, Cambridge, 1914.

27. Howland, J., and Marriott, W. McK.: *Bull. Johns Hopkins Hosp.*, 1916, **27**, 63.

28. Van Slyke, D. D., and Cullen, G. E.: *Jour. Biol. Chem.*, 1917, **30**, 289.

There is no evidence that the acidosis is caused by abnormal loss of alkali, for, as pointed out by Howland and Marriott, the analyses of diarrheal stools by Holt, Courtney and Fales show actually a loss of more acid than base. Nor can there be any significant loss of alkali in the urine, for both the hydrogen-ion concentration and the titrable acidity are increased.

Howland and Marriott concluded that the acidosis of diarrhea was probably dependent on defective elimination of acid by the kidney and suggested the possibility that it was due, in part, at least, to the failure of the kidney to eliminate acid sodium phosphate. Recently, they have found that there is a considerable increase in the inorganic phosphorus in the blood, which is in accord with this view.²⁹

The evidence derived from my own cases is entirely in accord with the view that the acidosis of intestinal intoxication is due to faulty elimination by the kidney. The blood has been examined for acetone bodies in six cases with severe acidosis, and in no case was the amount greater than could be accounted for by starvation. The greatest value was 37 mg. of total acetone bodies, determined as acetone, in 100 c.c. of blood.

In a great number of cases of relatively severe acidosis in intestinal intoxication, a single dose of sodium bicarbonate is sufficient permanently to correct the acidosis. It would seem most unlikely that this could occur if abnormal acids were being formed in large amounts. As an example the following protocol is given:

Protocol 1.—The patient, a boy, aged 6 months, was admitted Jan. 15, 1916. For two days before admission he had vomited almost every feeding and had many loose yellow stools. For twelve hours he had marked muscular twitchings, was semistuporous and refused all food. On admission the infant was somnolent, had distinct hyperpnea and seemed very ill.

Date	Carbon Dioxid Tension, Alveolar Air, Mm.	C.c. of CO ₂ , Reduced to 0,760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)
1/15	22	34.6
	3 gm. sodium bicarbonate by intravenous injection	
1/16	40	80.0
1/18	39	72.0
1/20	41	69.0
1/25	37	68.0

The hyperpnea disappeared entirely after the bicarbonate and the stupor lessened but did not disappear. The diarrhea continued until January 20, and during this period the infant was toxic and very ill. Improvement began January 20 and January 25 the infant was practically free from symptoms. A single dose of alkali was therefore sufficient to eliminate entirely a marked degree of acidosis.

29. Personal communication, Dr. John Howland, Dec. 11, 1917.

It might be suggested that in cases of this type the acid formation had perhaps occurred at a time before the patient came under observation and had ceased, so that the single dose of alkali was sufficient, merely because no acid formation was in progress at that time. Such objection, however, would be invalid in the cases in which the acidosis developed under observation. Five cases of this type have been studied, an example of which is given in illustration:

Protocol 2.—Case 22, boy, aged 10 months. The baby had from eight to ten loose stools daily for five days; the day before admission he refused all food and became somnolent. On admission he showed evidence of moderate fluid loss and his expression was dull. There was no hyperpnea. The development of acidosis is shown by the following data. On November 19 hyperpnea was noted.

Date	Carbon Dioxid Tension, Alveolar Air, Mm.	C.c. of CO ₂ , Reduced to 0, 760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)
11/14/16	36.0	64.0
11/16	36.0	65.1
11/17	30.0	
11/18	27.0	
11/19	23.0	38.0
	3.7 gm. sodium bicarbonate by intravenous injection	
11/20	40.0	87.0
11/21	42.0	
11/23	37.5	
11/25	37.5	80.0
Death		

In this case the acidosis developed under observation and was corrected by the administration of sodium bicarbonate. The hyperpnea disappeared; the other evidences of intoxication were influenced but little, and the infant died without further evidence of acidosis.

These observations are entirely in accord with the view that the acidosis is due to the failure of the kidney properly to fulfil its function of preserving the alkali reserve of the blood and contrary to its dependence on the formation of abnormal acids.

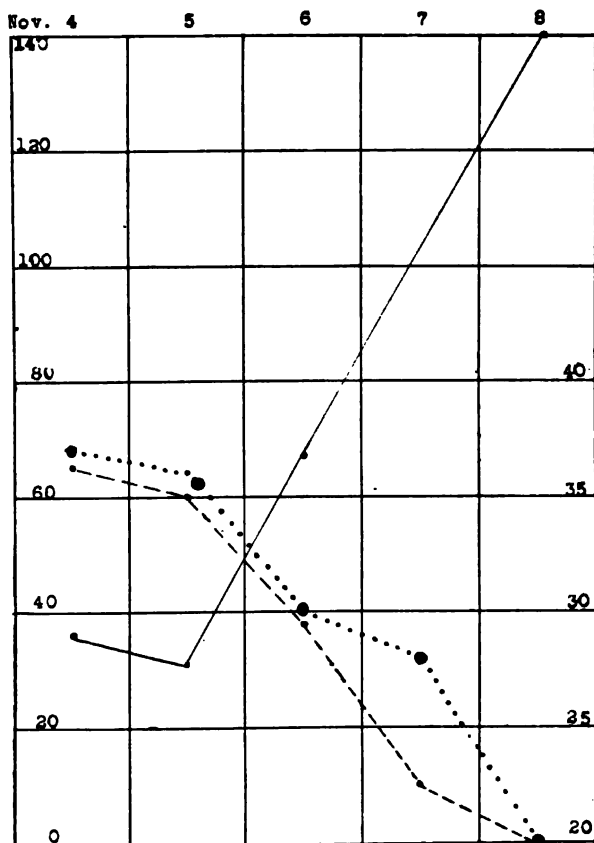
Evidence has been given which demonstrates that there is an accumulation of waste products in the blood due to defective secretion of urine. It seems only reasonable to suppose that the acidosis is of similar origin.

Six patients with intestinal intoxication have been observed to whom it was possible to supply approximately as much water as was lost. None of these patients showed a marked diminution in the excretion of urine and none developed acidosis.

In five cases the acidosis developed under observation. In three the output of urine was carefully observed, and in each instance the

acidosis was preceded by a diminished excretion of urine and the chemical evidence of impaired renal function. This occurrence is illustrated by the accompanying curve.

It would seem, therefore, that the acidosis of intestinal intoxication is probably due to defective kidney function.



Baby Y., aged 9 months. For three days previous to admission he appeared ill and passed from three to four loose green stools a day. During this period he vomited four times. On admission he was fairly nourished, the fontanel was not depressed and the skin was fairly moist and elastic. The infant was somnolent but could be roused easily. Until November 7 the food consisted of 3 ounces each of protein milk and barley gruel, given every four hours. In addition, large amounts of water were given. The stools were watery and from five to seven were passed in twenty-four hours. Vomiting became severe on November 8 and the food was changed to barley gruel. In the chart ----- with the figures at the left = urine in c.c. during a two-hour period after ingestion of 120 c.c. of water; ——— = nonprotein nitrogen of the blood in milligrams per 100 c.c.; with the figures at the left = carbon dioxid tension, in millimeters, of the alveolar air.

VI. THE SYMPTOMS OF INTESTINAL INTOXICATION

To determine definitely at present the origin of the symptoms of intestinal intoxication is obviously impossible, but there are facts bearing on this question which seem of sufficient importance to mention.

In a number of cases the acidosis bears a definite relation to the symptoms. This is quite evident when the symptoms disappear promptly after the correction of the acidosis by alkali. In some of the cases there is but little improvement in the symptoms after acidosis is eliminated. Hyperpnea, if present, always disappears, but at times the patient remains semistuporous and the prostration and other manifestations remain unchanged. Although in such cases the symptoms cannot be due directly to acidosis, yet it seems possible that the lack of alkaline reserve had caused injury to the tissue which is not repaired by the mere correction of the existing acidosis. Even granting the correctness of this assumption, there are cases of intestinal intoxication in which the symptoms are marked and yet acidosis is absent. The symptoms in these cases, except that hyperpnea is absent, seem identical with those of cases in which acidosis is present. This is also true of those cases in which the symptoms improve after the administration of alkali but return within a short time despite the fact that there is no recurrence of acidosis.

The improvement which occurs after the administration of sodium bicarbonate is probably not always due entirely to the alkali. Part is due to the water, and moreover, in the regular treatment of these cases, large amounts of water are given independently of alkali.

While there seems no question that acidosis is an important cause of the symptoms of intestinal intoxication, yet it is by no means the whole cause.

There is no evidence to indicate that the retained nitrogenous waste products are responsible for the symptoms. It is generally believed that in uremia, even with considerable nonprotein nitrogen retention, these substances are not responsible for the toxic symptoms. Recently, Hewlett, Gilbert and Wickett³⁰ were able to cause toxic symptoms in normal adults by feeding large amounts of urea. The symptoms, however, were slight in comparison to the degree of urea retention in the blood and as compared with what is often observed in uremia. These experiments show that large amounts of retained urea can be toxic, yet they do not demonstrate that the amount of urea retained in intestinal intoxication can be the cause of the toxemia.

There is a close analogy between intestinal intoxication and uremia. Indeed, all of the evidence points directly to the fact that their nature

30. Hewlett, A. W., Gilbert, Q. O., and Wickett, A. D.: *Arch. Int. Med.*, 1916, **18**, 636.

is essentially the same. In uremia the kidney fails to fulfil its proper function, due to an anatomic lesion. In intestinal intoxication the same result is brought about through loss of fluid. Waste products normally excreted by the kidneys are retained because there is insufficient water for diuresis.

Similar to uremia, based on symptomatology, there are two groups of cases of intestinal intoxication. In one group convulsions, involuntary muscular movements, muscular twitching and coma are present. The onset is usually acute and the infant is not greatly emaciated. Diarrhea may be slight and is absent in some cases. Food or water is usually refused and is vomited if taken.

In the second group the onset is less acute, but occurs following vomiting and diarrhea of some days' duration. Convulsions rarely occur and the infant is somnolent or semistuporous instead of comatose. Wasting is very marked and the patient presents the shrunken appearance which is so characteristic of great loss of fluid.

In both uremia and intestinal intoxication acidosis is a frequent occurrence.

Aside from the question of acidosis, intestinal intoxication similar to uremia appears to be some form of poisoning. Whether this poison is a product which the kidney has failed to excrete, whether it arises from disordered metabolism or is elaborated by bacterial growth in the intestinal tract, is one of the fundamental problems with which we are confronted.

SUMMARY

In intestinal intoxication there is a marked increase in the non-protein nitrogen and urea of the blood. This increase is not due directly to increased concentration of the blood from loss of water. The high nonprotein nitrogen and urea are due to defective kidney elimination.

The renal lesions in intestinal intoxication are not sufficient to account for the impaired elimination by the kidney. It is probably due to the fact that lack of water restricts the formation of urine. This condition is probably due to the following factors which may act singly or in combination: 1. The loss of water in the stools is so great that it is impossible for the infant to ingest sufficient fluid to replace the loss. 2. The patient refuses to ingest fluid or vomits practically all that is taken. As a result the tissues become dehydrated. The retention of nitrogenous waste products and the failure of the kidney to do its part in preserving the acid-base equilibrium results from the deficient secretion of urine. The oliguria may be due to the fact that the dehydrated tissues hold as much water as possible so that none is available for the formation of urine. Other factors, dependent mainly

on the loss of water, which may play a rôle are: 1, an increase in the concentration of blood colloids to such degree that their osmotic pressure is greater than the arterial pressure in the kidney; 2, a diminution in the total blood volume leading to decreased blood flow through the kidney.

The symptoms of intestinal intoxication are essentially those of uremia. The two conditions are similar in all essentials. In one, defective kidney function is due to an organic lesion; in the other it results from the negative water balance and consequent oliguria.

Acidosis plays a definite part in the symptomatology of intestinal intoxication, but the essential cause is probably some unknown toxic agency.

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It is with pleasure that I acknowledge my great indebtedness to Dr. L. E. La Fétra for the use of material from his service and for his stimulating interest in the work. I desire to thank Dr. Charles Norris for examining and describing the kidney sections. To Dr. A. O. Gettler, pathologic chemist, Bellevue Hospital, I am indebted for much advice and assistance. My thanks are due to Dr. W. R. May for much assistance during the early part of the work.

EFFECT OF BODY POSTURE ON THE POSITION AND EMPTYING TIME OF THE STOMACH *

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There is yet much to learn about the baby's digestive apparatus. Any knowledge added, no matter how small in amount, will bring us nearer the desired goal of maximum information. This work was undertaken by us on account of the scarcity of reports especially concerning the motility of the child's stomach under the varying influences of posture.

Observations on Positions of the Stomach.—Sixteen observations of the effect of body posture on the position of the stomach were made in four cases. The influence of gravity both on the shape of the stomach and the position of the meal is well demonstrated in the illustrations. The gas bubble, no matter what the position of the stomach may be, always rises to the highest point of the stomach. We noted in one of our patients that at the age of 3 years the stomach approximated the adult type both in form and position.

Observations on Motility.—Thirty-three observations were made in twelve cases. Comparative examinations were made in the prone, supine, erect, right lateral and left lateral positions. In one of our cases the stomach was empty at the end of two hours, in two cases at the end of two and one-half hours, and in one case at the end of three hours. We found in some of the cases that the food did not enter the duodenum immediately following feeding. Active peristalsis was noted with the fluoroscope as early as the fourth month of life (Case 10821).

Technic.—In making the observations a Coolidge tube was used with 2 milliamperes of current, spark gap 6 inches, and distance from target to screen 20 inches. The method employed was by screen tracings, which were adopted in preference to the roentgenographic method, because they permitted of greater accuracy and certainty of results and a saving of time, permitting observations of respiratory movements on the stomach and a study of peristalsis. The opaque meal consisted of, in addition to the child's customary meal, barium sulphate, the amount varying from 100 grains in the youngest child of 6 weeks to 1 ounce

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* Read before the Section on Diseases of Children at the Sixty-Eighth Annual Session of the American Medical Association, New York, June, 1917.

in a child 5 years old. The barium was thoroughly mixed with the food and in the cases of nursing infants the milk was withdrawn from the mother's breast in the quantity usually given by the mother to the baby as ascertained by weighing, barium mixed with it and the food given by bottle. In no instance was any untoward effect noticed in the children by reason of the addition of the barium. For the comparative observations of position of the stomach and motility, the meal and quantity in each individual case was the same. No attempt was made to test the exact time of emptying, on account of the variation

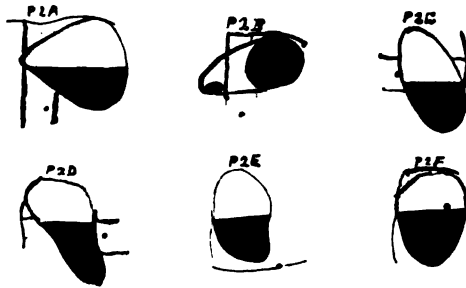


Fig. 1 (No. 10783).—Erect (P. A.) P2A; supine (P. A.) P2B; left lateral (P. A.) P2C; right lateral (P. A.) P2D; prone (right to left) P2E; supine (left to right) P2F.

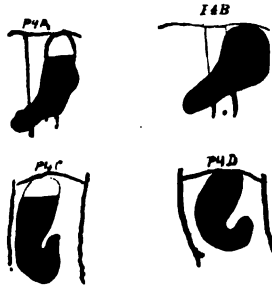


Fig. 2 (No. 10816).—Erect (P. A.) P4A; supine (P. A.) P4B; erect (right to left) P4C; right lateral (right to left) P4D.

in the ages of the children and the composition of the food, but rather the relative emptying time as influenced by the body posture. The screen tracings of motility were all made at the end of a fixed interval for each individual child and the final tracing, irrespective of the position of the stomach during emptying, was made with the patient supine with the rays directed postero-anteriorly. These tracings were photographed and made into slides.

With regard to the emptying time, immediately following the termination of each feeding the child was placed in the posture under consideration and maintained in that position for a fixed interval. All

children observed were in good health and their gain in weight was not interfered with.

ANALYSIS OF CASES

1. Comparison of right and left lateral positions: four cases. Right showed increased motility.

2. Comparison of right lateral and supine positions: five cases.

3. Comparison of right lateral and prone positions: two cases.

4. Comparison of right lateral and erect positions: four cases.

In all of the foregoing the motility of the stomach was increased in the right lateral compared with the other positions.

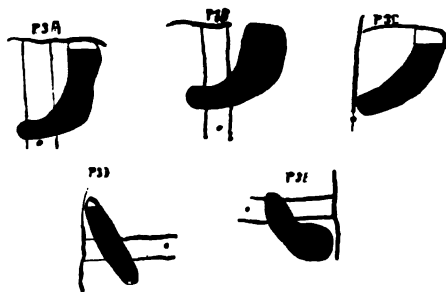


Fig. 3 (No. 10028).—Erect (P. A.) P3A; supine (P. A.) P3B; erect (right to left) P3C; right lateral (P. A.) P3D; left lateral (P. A.) P3E.



Fig. 4 (No. 10895).—Right lateral, no tracing, empty; supine 1A; prone 1B.

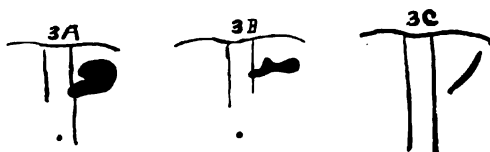


Fig. 5 (No. 10821).—Supine 3A; Prone 3B; erect 3C; active peristalsis.

5. Comparison of left lateral with supine position: five cases. In four of these the left lateral position showed greater motility. In one case there was no difference.

6. Comparison of left lateral with prone position. Two observations in the prone position were discontinued because of colic, so that comparisons could not be made.

7. Comparison of left lateral with erect position: four cases. Two of these were in favor of the left lateral position and two in favor of the erect position.

8. Comparison of the supine with the prone position: five cases. It was necessary to discontinue two of the observations in the prone position on account of the extreme colic experienced by the infants. Three other cases showed an increased motility in the prone position. One of these three infants also suffered from colic, but the position was maintained.

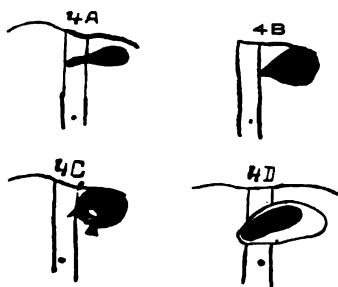


Fig. 6 (No. 10812).—Right lateral 4A; left lateral 4B; supine 4C; erect 4D.



Fig. 7 (No. 10623).—Right lateral, empty, no tracing; left lateral 5A; supine 5B; erect 5C.



Fig. 8 (No. 1100).—Right lateral 7A, empty; left lateral 7B, teething and fretful on day of left lateral; erect 7C.



Fig. 9 (No. 10830).—Right lateral 8A, empty; left lateral 8B; supine 8C.

9. Comparison of the supine with the erect position: six cases. Three of these were in favor of the supine position and three in favor of the erect position.

10. Comparison of the prone and erect positions: two cases. The prone posture showed increased motility as compared with the erect.

Table 1 shows the observations made on the position of the stomach, the posture of the child and the direction of the ray being indicated in each instance.

TABLE 1.—OBSERVATIONS ON POSITION

Number	Age	Food	Quantity, Ounces	Barium Drams	Position and Direction of Ray			
					Erect	Supine	Prone	Right Lateral
10783	4 mos.	Breast milk	4	2½	P. A.	P. A. S. D.	D. S.	P. A.
10829	8 yrs.	Cow's milk	8	6	P. A. D. S.	P. A.		P. A.
10816	5 yrs.	Cow's milk	8	8	P. A. D. S.	P. A.		D. S.
10812	4 mos.	Cow's milk, 33¼%	4	2½	P. A.			

P. A. = postero-anterior; D. S. = dextrosinistral; S. D. = sinistrodextral.

TABLE 2.—COMPARISON OF RESIDUE IN DIFFERENT POSTURES *

Number	Age	Quantity, Ounces	Food	Interval, Hours	Barium, Drams	Relative Amount of Residue Left				Remarks
						Right Lateral	Left Lateral	Supine	Prone	Erect
10812	4 mos.	4	Cow's milk, 33¼%	2	2½	1	2½	2½	†	1½
10823	7½ mos.	6	Breast milk	8	3	minus	1	2	...	2½
11000	10 mos.	8	Cow's milk, 50%	2½	3½	minus	2½	...	...	1
10880	15 mos.	8	Cow's milk, 50%	2½	4	minus	1	1½	...	
10783	4 mos.	4	Breast milk	2	2½	1	...	3	2	3½
10896	6 wks.	3	Cow's milk, 25%	2	100 gr.	minus	...	1½	1	
10921	2 7/12 yrs.	8	Cow's milk	3	6	...	1	1½	†	
10886	2½ yrs.	6	Cow's milk	3	4	...	minus	1½	...	1
10821	4 mos.	2½	Cow's milk, 50%	2	2½	...	...	2½	1	1½
10915	9 mos.	8	Cow's milk, 75%	2	3½	...	...	1	...	8

* One observation was made on each of two other cases, but as no comparative observations were made they were omitted.

† Observation discontinued because of colic.

Table 2 shows the observations made on motility, the relative amount of residue in the different postures being shown in each individual case.

CONCLUSIONS

1. The position of the stomach, and especially the position of the solid contents of the stomach, is influenced by body posture.
2. In one of our cases the age at which the adult type of stomach was reached was 3 years. (Case 10028.)
3. Motility of the stomach is most rapid in the right lateral position.
4. The supine position produces a comparatively slow motility.
5. Active peristalsis in the stomach was noted as early as the fourth month.

1776 State Street.

POLYCYSTIC KIDNEY IN AN INFANT *

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Cases of polycystic kidney observed in infancy, with necropsy findings, are still sufficiently rare to justify the report of the following case.

REPORT OF CASE

History.—E. S., of Syrian parentage, born July 1, 1916, of healthy parents. There were several other children in the family who were well and healthy. The family history was entirely negative. There was no history of miscarriages, no luetic history of any other kind and no known exposure to tuberculosis. The child was brought to the King's Daughters' visiting nurse clinic on July 28, 1916, then 4 weeks old.

Present Illness.—The mother said that she noticed before the child was 1 week old that its abdomen was unusually large, and that she thought it had grown since then. The child had appeared uncomfortable at times. There had been no vomiting. The stools had been regular, one to three per day, and on several occasions had contained small amounts of mucus. The child had nursed well and appeared satisfied with the breast. She thought the child passed more urine than most babies. The child was small and well developed, but emaciated. Otherwise than the stools there was nothing worthy of note.

Examination.—This showed a rather poorly developed child, though fairly well nourished; length, 19 inches; weight, 8 pounds 12 ounces; temperature, 98.6. The head appeared small (no measurements taken); the abdomen was quite large (17 inches in circumference); there were two masses present, one on each side of the umbilicus. These were apparent on inspection and palpation. They were distinctly nodular in outline and firm but movable, and appeared to arise from each side of the spinal column. They nearly filled both flanks and were dull to percussion, except when some folds of intestine, distended with gas, passed over them. The heart was negative. The liver was palpable about 1 cm. below the costal border. The spleen was not palpable. The von Pirquet test was negative and Wassermann $\pm$, which in our clinic is disregarded unless there are other symptoms which lead to suspicion, and in that event another test is made.

The blood showed as follows: Hemoglobin, 60 per cent.; white blood cells, 14,000; red blood cells not counted; polynuclear cells, 55 per cent.; lymphocytes, 42 per cent.; eosinophils, 2 per cent.

The urine, which was examined repeatedly while the child was under observation, was uniformly negative, with the exception of one time, when a faint trace of albumin was reported. The urine, however, was never obtained in large enough quantities to determine the specific gravity, although the child always appeared to pass rather large amounts.

The subsequent history is of small moment. The child continued to nurse well and the milk was of good quality. Weighing before and after nursing showed that the child received from 2 ounces on admission to 4 ounces just before death. In spite of this the child did not grow in length or increase in weight. The latter, on the day before death, was 7 pounds 13 ounces. The temperature varied little and never exceeded 100 F. (during a mild attack of

* Submitted for publication Dec. 21, 1917.

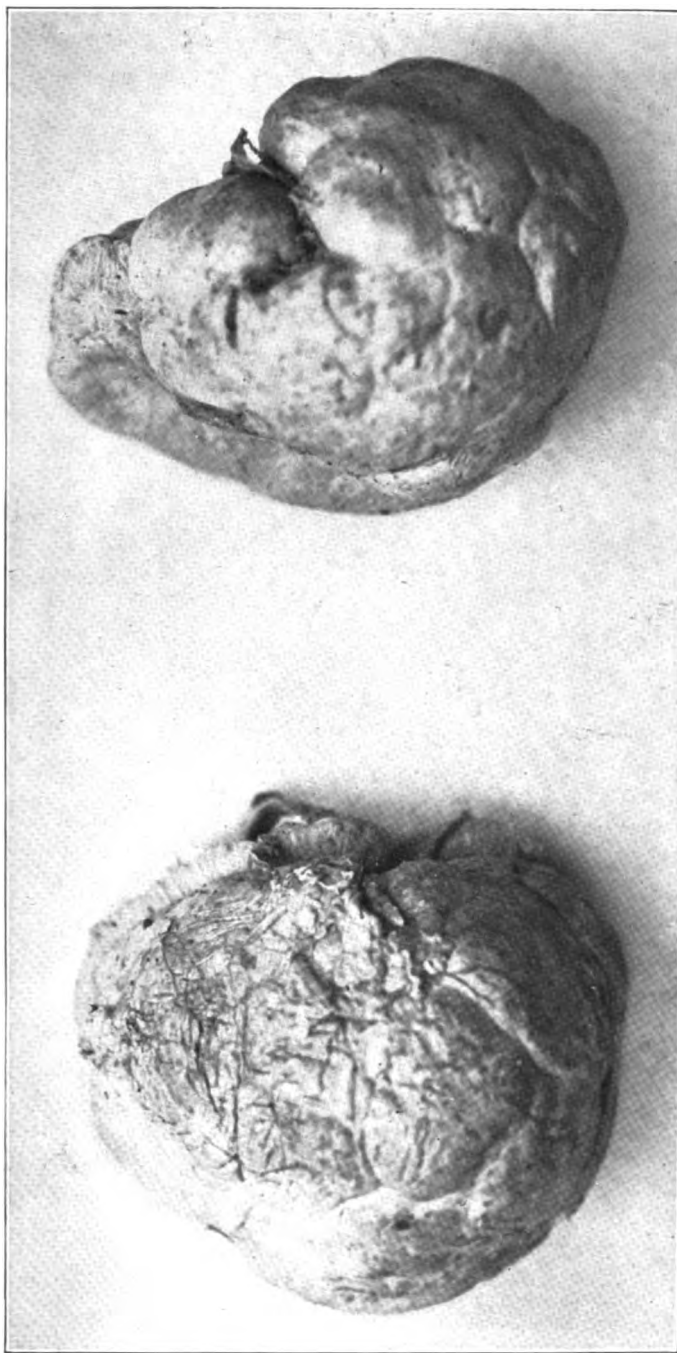


Fig. 1.—Photographs of kidneys, not taken until hardened. Size of each when fresh, 10 by 7 by 3 cm.; weight, right, 200 gm.; left, 180 gm.

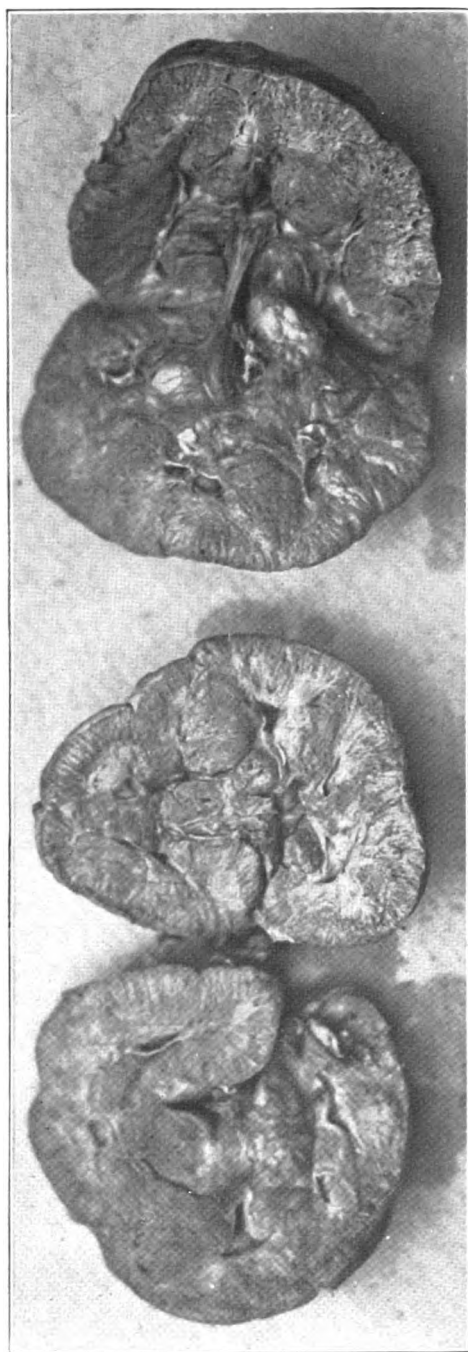


Fig. 2.—Photographs of kidneys laid open showing the gross pathology.

bronchitis). During the last months of life the child was very restless, appearing uncomfortable most of the time, and the mother thought there was pain.

Diagnosis.—From the negative von Pirquet, the very doubtful Wassermann and the good family history, both tuberculosis and syphilis were at once rejected. It seemed, therefore, that the diagnosis lay between sarcoma of the kidney and

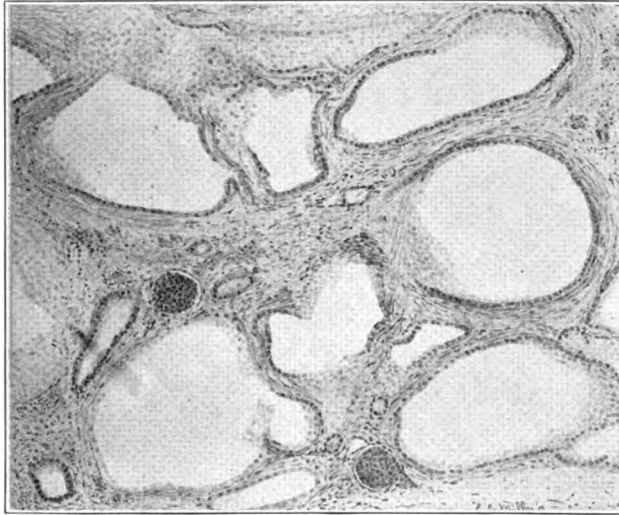


Fig. 3.—Drawing of a section of the cystic kidney, $\times 75$. $\times 150$.

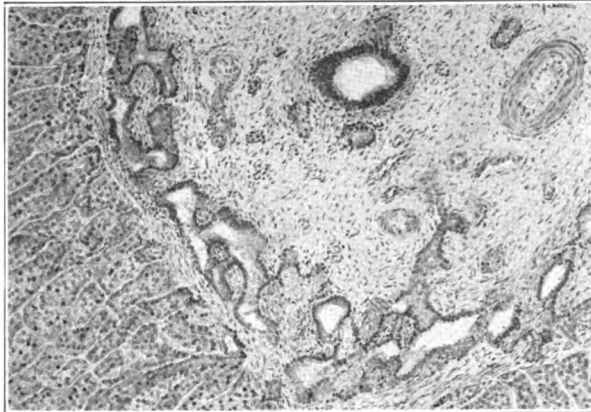


Fig. 4.—Drawing of section of liver, $\times 75$. $\times 150$.

polycystic kidney. Bilateral tumors of irregular outline, dating from birth, point strongly toward polycystic kidney. We therefore made this as the probable diagnosis. The parents suggested an operation, but we felt that this was not justified.

The patient was exhibited before the Norfolk County Medical Society as a case of polycystic kidney. The child died, Feb. 27, 1917, when 8 months old.

Necropsy.—This was performed by Dr. R. S. Kight. The pathological findings are as reported by Dr. Mary E. Roche, pathologist to the clinic.

A male child, aged 8 months; length, 20 inches; body very much emaciated; weight (just prior to death), 7 pounds 13 ounces; no subcutaneous fat. Heart not enlarged; abdomen distended. Lungs: Hypertrophic congestion over posterior surface of both lungs; no enlargement of bronchial lymph nodes. Abdomen: Colon distended with gas; peritoneum adherent to tumor masses in both sides of abdomen.

Kidneys: Enlarged, completely filling both sides of the abdominal cavity posteriorly from the liver to below the crest of ilium. Each kidney measured 10 by 7 by 3 cm., and was of grayish color. They weighed 200 and 180 gm., respectively. The external surface was rough, showing raised, lobulated areas. The capsules were thickened and adherent to the kidney substance. The kidneys were soft and elastic, the surface covered with cystic elevations, varying in size from 2 mm. to 1 cm. in diameter. On section, the cut surface was grayish, translucent, and yellowish watery fluid exuded from the cystic areas. White connective tissue bundles radiated from the pelvis toward the cortex. The cortex was about 1 cm. thick, with coarse striations running into the pyramids.

Liver: This organ did not extend below the costal margin. The surface was rough and nodular, resembling atrophic cirrhosis. On section the connective tissue was much increased, the capsule thickened, and cut with resistance. Microscopic frozen sections showed atrophied liver cells and much connective tissue.

Taylor Building.

ACUTE SYPHILITIC MENINGITIS IN AN INFANT TWELVE MONTHS OLD*

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Acute syphilitic meningitis has been recognized as a clinical entity since the year 1855,¹ but it was not until 1902² that the changes in the spinal fluid of this disease were observed. Ravaut,³ writing in 1903, took the ground that syphilis in the secondary stage was a true septicemia, the skin and nervous system being principally affected. Whenever there were definite meningeal symptoms he found an increased number of lymphocytes in the spinal fluid.

The cytology of the spinal fluid was then studied rather extensively during the next ten years by the French writers. It was found that occasionally an increased number of lymphocytes was present in the spinal fluid, not only in the secondary stage of acquired syphilis, but also in hereditary syphilis (Tobler,⁴ Ravaut and Ponselle⁵). The increase in the number of lymphocytes was found whenever there were meningeal symptoms, but occasionally when there were none.

A marked increase of the lymphocytes in the spinal fluid with a positive reaction for globulin suggested in these cases the presence of a syphilitic meningitis.

Sézary⁶ has therefore divided the clinical manifestations of syphilitic meningitis, whether occurring in the acquired or hereditary type of syphilis, into three groups: (1) A latent form in which there are the general evidences of syphilis but no symptoms of meningitis; the spinal fluid in these cases is under increased tension; the cells are numerous and the globulin test positive. (2) A true meningitis: this condition is quite rare and presents the general symptoms and spinal fluid changes of an acute meningitis. (3) A more severe type which resembles an acute meningo-encephalitis: these patients have high fever, convulsions, marked rigidity of the neck and frequently localized paralyses, especially of the face and ocular muscles.

The great majority of cases of acute syphilitic meningitis, belonging to the second group described, have been observed in young adults.

* Submitted for publication Jan. 5, 1918.

* From the Babies' Hospital.

1. Reported by Bonnet and Goujat: *Lyon méd.*, 1910, **114**, 549.

2. Milian, Crouzon and Paris: *Bull. Soc. méd.*, Paris, 1902, **19**, 117.

3. Ravaut: *Ann. d. dermat. et de syph.*, 1903, **4**, 537.

4. Tobler: *Jahrb. f. Kinderh.*, 1906, **64**, 1.

5. Ravaut and Ponselle: *Bull. et mém. Soc. méd. d. hôp., de Paris*, 1906, **23**, 3.

6. Sézary, A.: *Jour. méd. Franc., Par.*, 1913, **7**, 201.

In these cases the meningitis is usually secondary to an acquired syphilis. A few examples of acute syphilitic meningitis secondary to hereditary syphilis have, however, been reported.

Ravaut and Darré⁷ were probably the first to report an example of this type with an extensive study of the changes in the spinal fluid: the infant was 3 weeks of age when first observed and presented the general manifestations of hereditary syphilis. During the first year the child had four separate and distinct attacks of meningitis. Spinal puncture greatly relieved the meningeal symptoms; in each instance the fluid was under increased tension, the lymphocytes numerous and the globulin test positive. During the second year the child remained healthy and several spinal punctures revealed a normal fluid.

A few years later Hutinel⁸ stated that syphilitic meningitis occurs in infants, associated with such specific lesions as pemphigus, roseola and changes in the bones, liver and spleen. He quotes another example of this condition, observed by Ravaut, in an infant 3 weeks of age who presented scattered syphilids over the trunk and face, a hard liver and large spleen. There were observed numerous convulsions, a tense fontanel, and the spinal fluid showed a markedly increased number of lymphocytes. The diagnosis was confirmed by necropsy, numerous spirochetes being found in the exudate at the base of the brain.

REPORT OF CASE

History.—H. M., a male child, 12 months of age, was admitted to the Babies' Hospital June 7, 1916. The mother appeared healthy and denied having had syphilis; but the father, several years previously, had been treated for that disease. There had been four infants born at the seventh month of pregnancy before the birth of the patient. The first lived for five days; the second and third were stillborn, and the fourth lived but four days. The patient was born at term and appeared healthy. No history could be obtained from the mother, who was fairly intelligent, of any early manifestations of hereditary syphilis, or in fact any signs up to the time of admission. The infant was nursed for only five weeks, but later gained normally on modified milk mixtures, and at the time of admission weighed 18 pounds.

The first symptoms of the present illness occurred two weeks before admission; the child vomited several times a day and the bowels were constipated. Most of the food had been refused for a week, and for three days before admission there was a gradually increasing drowsiness. There was no history of fever or convulsions.

Examination.—On examination the child lay with head slightly retracted and breathing regularly. He took very little notice of his surroundings; was dull but not stupid. There were no lesions of the skin or the mucous membranes. The fontanel was tense but not bulging. There was definite but slight rigidity of the neck; pulse rate 100 and very slightly irregular; the spleen was not palpable, but the liver was felt at the costal margin; the epitrochlear glands were readily palpable; the knee jerks active and equal on both sides.

7. Ravaut and Darré: *Gaz. d. hôp., Par.*, 1907, **80**, 207.

8. Hutinel: *Rev. gén. de clin. et de therap., Par.*, 1913, **27**, 437.

The patient lived for four days; the drowsiness deepening into coma, in which condition he died without convulsions. The vomiting continued about once a day. The temperature remained practically normal until the day before death when it rose to 102 F. The blood count on admission was 17,700 leukocytes, 86 per cent. of which were polymorphonuclears and 14 per cent. lymphocytes. A second count four days later showed 18,200 with 71 per cent. polymorphonuclears and 29 per cent. lymphocytes. Three von Pirquet skin tests were negative.

About 15 c.c. of a slightly turbid spinal fluid were withdrawn by spinal puncture under moderately increased pressure. The cells numbered 650 per cm., 66 per cent. of these being lymphocytes. The globulin was moderately increased. Three subsequent spinal punctures gave practically the same results. Cultures made from the spinal fluid were negative in every instance and no tubercle bacilli could be found in the smears after a prolonged search.

On the third day after admission an examination of the eyegrounds by Dr. E. F. Krug revealed the presence of a typical syphilitic choroiditis. As a result of this finding the spinal fluid was examined for spirochetes. Smears were made from the sediment of centrifugalized specimens. Some were prepared by the India-ink method and others were stained with the Giemsa stain. Numerous spirochetes were found by both methods. They were confirmed by similar findings made on the following day from a fresh sample of spinal fluid. The Wassermann reaction was strongly positive in both the blood and spinal fluids. A single dose of diarsenol was given intravenously, but the child by this time was almost moribund and died the next day.

Necropsy.—(By Dr. Martha Wollstein.) The meninges were everywhere congested and the surface of the brain slightly compressed, especially over the left hemisphere. The pia was opaque in appearance and moderately edematous; more marked over the frontal lobes. There were small, irregular patches of grayish-white exudate covering the blood vessels in the sulci of the parietal and temporal lobes. This condition was most marked over the left temporal lobe and extending along the left sylvian fissure. There was nowhere seen any fibrinopurulent exudate as in meningococcus or pneumococcus meningitis, but the plaques resembled those sometimes seen in old meningococcus inflammations. The brain substance beneath showed considerable softening. The gray matter was studded with minute hemorrhages, and several small vessels showed the presence of minute thrombi. There was dilatation of the ventricles, with a slightly turbid fluid, especially on the left side. The floor of the posterior cornu of the left lateral ventricle showed many minute hemorrhages, two small thrombosed vessels and an early stage of softening. The right lateral ventricle was very slightly larger than normal and the floor of the anterior cornu showed some minute grayish-white plaques about 2 to 3 mm. in diameter.

Smears made from the exudate on the surface of the brain and from that in the ventricle all showed the presence of numerous spirochetes.

The heart was not enlarged; the endocardium of the left ventricle showed thickened grayish areas, more marked just below the aortic valve; the myocardium and valves appeared normal.

The liver was rather small; the capsule, especially along the upper surface, was thickened; there were also seen many subcapsular hemorrhages; the substance of the liver was firm, slightly fatty in some places and congested in others; the connective tissue was thickened throughout the organ. The lesion was essentially a syphilitic hepatitis.

DISCUSSION

The clinical picture presented by this infant closely resembled that of tuberculous meningitis. The gradual onset, the vomiting, the constipation and drowsiness were all typical of that disease. Even in spite of three negative tuberculin skin tests and a diligent search for tubercle

bacilli in the spinal fluid, it was thought probable that the case might still be tuberculous in origin. It was in the search for choroid tubercles that the first suggestion was obtained as to the true nature of the disease; and this led to an examination of the spinal fluid for spirochetes. From the presence of these in numbers the diagnosis was established.

It was now apparent that the symptoms differed in some important respects from those of tuberculous meningitis: the continued absence of fever and convulsions, the turbidity of the spinal fluid and the relatively small percentage of lymphocytes.

In other turbid spinal fluids, pyogenic organisms are regularly found. None were present in this case, either by smear or culture.

Acute syphilitic meningitis in infants is a very rare condition and probably not more than half a dozen cases have been reported. In those cases which come to necropsy the spirochetes were demonstrated in the exudate at the base of the brain. But in the recent reviews of acute syphilitic meningitis by Bonnet and Goujat,¹ Miriel,⁹ Jeanselme and Chevallier,¹⁰ Desneux, Dujardin and Weil,¹¹ and Bonnet¹² not a single instance is recorded in which the spirochetes were demonstrated during life in this disease in infancy.

I am greatly indebted to Dr. L. Emmett Holt for permission to publish this report.

9. Miriel, M.: *Gaz. d. hôp., Par.*, 1911, **84**, 15.

10. Jeanselme and Chevallier: *Rev. de méd., Par.*, 1912, **32**, 329.

11. Desneux, Dujardin and Weil: *Jour. méd. de Brux.*, 1913, **18**, 175.

12. Bonnet: *Lyon méd.*, 1915, **124**, 55.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF LITERATURE ON TUBERCULOSIS IN CHILDREN, 1917 *

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MODE OF INFECTION

1. Weber, F. P.: Congenital Tuberculosis. *Brit. Jour. Child. Dis.*, 1916, **12**, 321 and 359.
2. Park, W. H.: Channels of Infection and Methods of Transmission of Tuberculosis, *New York Med. Jour.*, 1917, **105**, 777.
3. Klotz, O.: Portal of Entry and Route of Infection in Tuberculosis in Children. *Pennsylvania Med. Jour.*, 1917, **20**, 811.
4. Opie, E. L.: Relation of Apical Tuberculosis of Adults to Focal Tuberculosis of Children and Adults. *Jour. Exper. Med.*, 1917, **26**, 263.
5. Opie, E. L.: Focal Pulmonary Tuberculosis of Children and Adults. *Jour. Exper. Med.*, 1917, **25**, 855.

F: Parkes Weber¹ reviews the literature on congenital tuberculosis, due to intrauterine infection by way of the placenta and fetal membranes. He says that genuine cases of congenital tuberculosis in human beings are undoubtedly rare, and it has been thought that they occurred only when the mother was in an advanced stage of tuberculosis, but more recent observations seem to show that placental tuberculosis may likewise develop when the mother's tuberculosis is not far advanced or is even latent or quiescent. The author's review includes thirty-three cases of true congenital tuberculosis, but he quotes the analysis of the subject by Pehu and Chalier who admit fifty-one cases as conclusively genuine and satisfying all critical demands. According to Pehu and Chalier, in cases of congenital tuberculosis in the infected fetus or infant there are generally tuberculous lesions to be seen in the organs, but in some cases, in spite of no pathologic-anatomic changes having been found, the fetal blood contains virulent tubercle bacilli. This latter condition is the status bacillaris of Honl and is to be distinguished from the actual presence of tuberculous lesions in the fetus.

Weber finds a difference of opinion as to the time of infection in these congenital cases. Pehu and Chalier say placental tuberculosis apparently does not occur until the fourth month of pregnancy. In this connection Pankow's work is of special interest. In twenty pregnant tuberculous women artificial abortion was brought about in the

* Submitted for publication Jan. 15, 1918.

third or fourth month of pregnancy, and from all these cases fetal pulp was injected into guinea-pigs without giving rise to tuberculosis. Dufour and Thiers, however, report the instance of a young woman who died of tuberculosis in the third or the fourth month of pregnancy. The placenta appeared to be healthy, and examination for tubercle bacilli in it gave negative results; but the peritoneum of the fetus contained fluid, animal inoculation with which gave rise to tuberculosis.

W. H. Park,² discussing the channels and methods of transmission of tuberculous infection, says two types of tubercle bacillus cause the disease in man, the human and the bovine. In New York City during the four or five years that pasteurized milk has been more generally used there has been a marked reduction in the percentage of bovine infection among children, and on occurrence it has been found among children fed raw milk. Park thinks droplet infection is more important than that from dried sputum, and the dust of the rooms inhabited by tuberculous persons is only slightly or moderately infected with tubercle bacilli. However, when the sputum clings to lips, fingers or clothing of the patient, there is danger of the bacilli being conveyed to another person. When the contact is close, as when the mother nurses her infant, the danger is very great; when limited, as shaking hands, handling furniture or clothing, it is slight. Although living tubercle bacilli are found more or less abundantly in the feces of all patients with human or bovine open tuberculosis and although many reach the water supply, the danger from the water supply is slight.

O. Klotz³ says that in spite of the tremendous amount of work done on all phases of the tuberculosis problem, there is no agreement on the question of the mode of infection. In order to throw more light on this subject he has searched for the tuberculous focus at 477 necropsies. A tuberculous process was met with in 170 cases of these 477, giving a percentage of 35. From his observations on these cases the author thinks there is no gainsaying the fact that the greatest incidence of tuberculosis is within the thorax, as compared with other parts of the body. This is true of all periods of life, even though in early childhood apparently a greater frequency of tuberculosis has been found in the bowel and its appendages. The closer analysis of the statistics of tuberculosis in childhood has recently indicated that the greater incidence of abdominal tuberculosis is not correct, when an impartial search is given to other parts of the body.

E. L. Opie⁴ has attempted to show the relation of phthisis in adults to tuberculous infection in childhood. In order to do this he has studied the pathology of tuberculosis in children and adults and obtained data as to the frequency of infection among them. During

the first two years of life massive tuberculous lesions sometimes implicate a considerable part of one lung, but do not affect the apex more frequently than other parts. Lesions at this time exhibit no tendency to heal. After the end of the second year tuberculous lesions are usually small, seldom more than 1.5 mm. in diameter, and may be situated in any part of the lung substance. They may be designated as focal lesions and differ from the lesions of infancy only in size. They show, however, a tendency to heal, which is indicated by encapsulation of the caseous focus with fibrous tissue. The caseous material may undergo calcification and become surrounded by a fibrous capsule. The author found that nearly two thirds of all these tuberculous foci have been in contact with the pleural surface of the lung. The lesions are scattered impartially throughout the lungs. The most conspicuous characteristic of tuberculosis in children is the extent of involvement of the regional lymph nodes, but the author agrees with Ghon that the pulmonary lesion is primary and the lymphatic foci are secondary. Masses of greatly enlarged caseous lymphatic glands may occupy the hilus of the lung, in which is located the primary focus, and similar masses fill the spaces between the trachea and lungs or lie in the angle at the bifurcation of the trachea. As the age of the child increases there is less enlargement and caseation, and between the ages of 10 and 18 it is not uncommon to find small or calcified nodules in only one or two lymph nodes.

In adults tuberculous lesions of the lungs may be separated into two sharply defined groups: (1) lesions occupying the apexes of the lungs, tending to spread diffusely through the tissue of the apex and unaccompanied by caseation of the regional lymphatic nodes; (2) circumscribed lesions situated in any part of the lungs and accompanied by similar lesions of the regional lymph glands. In the lungs of adults who have died of disease other than tuberculosis this is the commonest type of tuberculous lesion. They have the distribution and characters of the circumscribed tuberculous lesions, which begin to appear after the second year of life and during later childhood and may be designated as focal tuberculosis. It is noteworthy that the incidence of focal tuberculosis increases continuously after the second year of life, and that at least 92 per cent. of all adults possess focal lesions. Focal tuberculosis is frequently fatal in early childhood, but after the tenth year it is rarely the cause of death. The existence of focal lesions does not preclude the occurrence of apical tuberculosis. Primary infection in almost all individuals who reach adult life occurs in childhood and has the characters of primary infection in animals, since it tends to implicate the regional lymph nodes. Koch showed that a secondary infection of an animal already tuberculous has a greater tendency to heal and does not extend to the regional lymph nodes, and this has

been confirmed by numerous observers. Apical tuberculosis usually exhibits the characteristics of secondary infection, since it pursues a chronic course and is usually unaccompanied by tuberculosis of the regional lymph glands.

Opie concludes, then, that focal tuberculosis of adults is identical with tuberculosis of childhood. It occurs in at least 92 per cent. of all adults. It may be acquired between the ages of 2 and 10, but in more than half of all individuals (in St. Louis) it makes its appearance between the ages of 10 and 18 years. Tuberculosis of childhood does not select the apexes of the lungs, is accompanied by massive tuberculosis of the regional lymph nodes, and exhibits the characteristics of tuberculosis in a freshly infected animal, while the tuberculosis which occurs in the pulmonary apexes of adults has the characters of a secondary infection. Almost all human beings are spontaneously "vaccinated" with tuberculosis before they reach adult life.

The following observations, E. L. Opie⁵ believes, also indicate that apical tuberculosis of adults is not the result of infantile tuberculosis, but is caused by subsequent infection: (a) Apical tuberculosis does not have its highest incidence, in accordance with common belief, in early adult life when focal infections acquired in childhood are relatively fresh and active, but is more common in later life, when the focal lesions of childhood have in most instances completely healed. Most of these apical lesions of later life pursue a chronic course and are discovered at necropsy in individuals who have died from other causes; (b) the well characterized lesions of tuberculosis acquired in childhood and found in adults with apical lesions are almost invariably calcified and healed. The apical lesion is in most instances relatively fresh and caseous, while the focal pulmonary lesion and associated lesions of regional lymphatic nodes exhibit no evidence of activity; (c) in a large proportion of instances of associated focal and apical tuberculosis the focal lesion is in one lung, but the apical lesion is limited to the opposite apex. This relation affords no support to the view that tuberculous lesions may be transmitted to the apex by way of the lymphatics.

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8. Ravenel, M. P.: The Transmission of Bovine Tuberculosis to Human Beings. *Arch. Pediat.*, 1917, **34**, 137.

9. Mitchell, A. P.: Primary Tuberculosis of Faucial Tonsil. *Jour. Path. and Bacteriol.*, 1917, **21**, 248.

10. Griffith, A. S.: Types of Tubercle Bacilli in Cervical and Axillary Adenitis. *Lancet*, London, 1917, **1**, 216.

11. Shimer, W.: Relation of Cow's Milk to Human Tuberculosis. *Indiana State Med. Assn. Jour.*, 1917, **10**, 193.

12. Wang, S. L., and Coonley, F.: Tubercle Bacilli in Breast Milk of Tuberculous Women. *Jour. Am. Med. Assn.*, 1917, **69**, 531.

C. Y. Wang⁶ has undertaken a study with the object of obtaining information as to the relative incidence of the human and bovine types of tubercle bacilli in the infection of man, irrespective of age and the nature of the tuberculous disease. The material was obtained from the pathologic department of the Royal Infirmary and Edinburgh Royal Hospital for sick children. One hundred and twenty-three strains of tubercle bacilli from 88 cases of tuberculosis were studied. All strains were found to conform in important respects to either the human or the bovine type of tubercle bacillus. In no instance was an atypical strain found. Of 68 cases of tuberculosis in adults, bovine tubercle bacilli were found in 7 instances, namely, from 1, of 29 cases of pulmonary tuberculosis, from 2 of 4 cases of abdominal tuberculosis, from 2 of 7 cases of generalized tuberculosis, and from 2 of 28 cases in which the only signs of tuberculosis were calcareous or caseous lesions. Three of the cases of bovine infection gave indication on postmortem examination that the path of infection was by way of the intestine. Of 20 cases of tuberculosis in children, bovine tubercle bacilli were isolated in 11 instances, namely, from 3 of 4 cases of abdominal tuberculosis, from 3 of 5 cases of tuberculous meningitis, and from 2 of 8 cases showing at necropsy no other evidence of tuberculosis than calcareous or caseous glands. In 9 of these cases of bovine infection the primary site of infection was in the intestine, as determined by postmortem examination. These bacteriologic findings confirm those of Fraser and Mitchell and emphasize again the great prevalence of bovine tuberculous infection in Edinburgh, especially among children.

Wang thinks the finding of a large percentage of tuberculous milk in Edinburgh explains only in part this high incidence of bovine tuberculosis there. He thinks the consumption of unboiled milk by the infant population is another very important factor. Investigation has shown that the diet of most children belonging to the working class consisted partly or wholly of cow's milk, and in only a small percentage was the milk boiled. Moreover, it was found that more children who were fed on raw milk gave a positive tuberculin test than those fed boiled milk.

In view of these facts Wang asserts that any measure resorted to in combating the disease should be directed not only against human spread of infection, but also against bovine source of infection. An adequate supervision of milk supply failing, the most efficient way of

safeguarding against the bovine type of tubercle bacillus is to subject all cow's milk for consumption to the process of boiling.

A. S. Griffith⁷ in summarizing the work of the British Commission on Tuberculosis found that in 930 cases of tuberculosis occurring at all ages the bovine bacillus was the infecting organism in 18.17 per cent. One hundred and ninety-six, or 34.2 per cent., of these cases occurred in children up to 5 years; 265, or 26.8 per cent., in children between 5 and 10 years; 127, or 12.6 per cent., in children between 10 and 16 years, and 341, or 5.9 per cent., in individuals above 16 years.

M. P. Ravenel⁸ reviews the work done in the matter of transmission of bovine tubercle bacilli to human beings and regards it as a mistake to emphasize too strongly that the danger from bovine infection is greater in early life. He has been forced to the conclusion that infection of adults with the human tubercle bacillus is much less common than was formerly believed and thinks it possible that further studies, considering the relative proportion of human and bovine infection, will show that adults are infected with the bovine tubercle bacillus relatively as frequently as with the human. Moreover, Ravenel does not believe that the portal of entry of the tubercle bacillus can be told from what is considered the oldest lesion—for example, that cases are of inhalation origin when the pulmonary lesions are the most advanced in the body. In animals it has been conclusively shown that pulmonary tuberculosis can be easily produced both by feeding and by injection of tubercle bacilli directly into the stomach, and the oldest lesions are found in the lungs after infection of known intestinal origin. It seems almost certain that the same thing may take place in children.

A. Philip Mitchell⁹ has attempted to ascertain the frequency of primary tuberculosis of the faucial tonsils and its relation to other tuberculous affections, especially to tuberculosis of the cervical lymph nodes. His study has consisted of examination of tonsils removed from children affected with tuberculosis of the upper deep cervical glands, and of hypertrophied tonsils removed from children with no clinical evidence of tuberculosis of the lymph nodes or other structures. The methods employed were histologic examination of the tonsils and inoculation of tonsillar tissue into guinea-pigs. The author thinks that histologic examination of the entire tonsil is a reliable diagnostic method, but he employs animal inoculations, also, to meet the criticism of those who maintain that foreign substances in the tonsils are frequently the cause of lesions identical with those produced by tuberculosis. Moreover, animal inoculations were necessary to determine the relative frequency of the human and bovine type of tubercle bacillus present in tuberculous tonsils.

There were 106 cases in which the tonsils were removed at operation for tuberculosis of the cervical glands. Of these, 51 cases were in children under 5 years, 49 cases in children between 5 and 15 years, and 6 cases were in adults. In 41 cases there were undoubtedly tuberculous lesions in the tonsils and 38 of these were in children. Inoculation tests were made in 92 of the 106 cases and positive results obtained in 20 cases. In 16 cases the bovine bacillus was obtained and in 4 the human type of tubercle bacillus was obtained.

There were 100 cases in which the faucial tonsils were removed for chronic hypertrophy and 9, or 9 per cent., yielded positive results when inoculated into guinea-pigs. The bovine bacillus was present in 4 cases, and the human in 2 cases, and in the other 3 cases the type was not determined.

Mitchell thinks the interpretation of these bacteriologic findings impossible without considering the source of infection. In a previous investigation he examined 406 samples of milk and in 82, or 20 per cent., he found tubercle bacilli. Children being large consumers of milk, it is quite clear how contaminated milk may be to them a frequent source of infection. In this connection it must be mentioned that 90 per cent. of the children under 5 years of age were bottle fed infants. Among children with tuberculous cervical adenitis, human source of infection seems very frequently absent. In not a single instance of bovine tonsillar infection in this series was there a history of pulmonary tuberculosis in other members of the household.

Mitchell draws the following conclusions from his study: 1. Tuberculosis of the upper deep cervical glands develops from a primary focus in the faucial tonsils much more frequently than is generally supposed. 2. Primary tuberculosis of the tonsils can be recognized only by the aid of the microscope and by inoculation experiments. The lesions are found immediately under the surface epithelium and near the mouth of the lacunae and in relation to the deeper portions of crypts or deep in the tonsils close to the capsule. The first mentioned site furnishes the greatest number of examples. 3. Hypertrophied faucial tonsils are the seat of primary tuberculosis, though rarely, as compared with tonsils from cases of tuberculous cervical adenitis. 4. Experimental results indicated that in Scotland primary tuberculosis of the faucial tonsils must be attributed to the drinking of milk from tuberculous cows, rather than to the inhalation of the tubercle bacillus conveyed by dried sputum or moist spray of a consumptive patient. 5. Bovine and human types of tubercle bacilli are present in the crypts of a small percentage of children without demonstrable tuberculous lesions either in the tonsils or elsewhere. 6. Tonsillectomy is essential in all cases of tuberculous cervical adenitis in chil-

dren. 7. The prognosis is very slightly influenced in children in whom the faucial tonsils and cervical glands are simultaneously affected with tuberculosis. 8. The difficulties associated with the reform of the milk supply and the lengthened period which must elapse before it becomes possible to obtain milk free from tubercle bacilli demand some means of rendering milk safe. The only safeguard is to be had in sterilization by boiling.

Since his last report on bacteriologic findings in cervical adenitis, A. S. Griffith¹⁰ has studied fifty-two additional cases in order to ascertain the type of infecting organism. In seventeen of the cases no tubercle bacilli were found and inoculations into guinea-pigs were negative. In thirty-five cases cultures of tubercle bacilli were isolated either from the original material or from material obtained after the inoculation of guinea-pigs. In fifteen of the thirty-five cases the cultures showed the bovine tubercle bacillus. In nineteen cases the human bacillus was isolated and in three the strain was atypical. The author's figures show that in children under 10 years cervical gland tuberculosis is caused more frequently by the bovine than by the human type of tubercle bacillus, for three fourths of the cases in children under 10 years yielded the bovine type of organism. In persons over 10 years infection of human origin is more common, for in only one third of the individuals from 10 to 20 years was the bovine organism obtained, and in rather less than one fifth of the cases in persons over 20 years.

W. Shimer¹¹ has studied the relation of cow's milk to human tuberculosis. According to the author's statistics, one dairy cow of every ten has tuberculosis (i. e., in Indiana). Hence, if every dairy man kept ten or more cows and mixed the milk, all of the milk would contain tubercle bacilli. Cows rarely suffer from tuberculosis of the udders, and Shimer thinks the chief source of the tubercle bacilli is the feces. Most market milk contains manure, and there are always tubercle bacilli in the manure of cows with tuberculosis, as they invariably swallow their sputum. Cream is one of the greatest sources of danger. Cream contains a concentration of tubercle bacilli and is made into butter. The interval of time which elapses between the production and use of cream and cream products is so short that the bacilli retain their virulence. As long as raw milk from tuberculous cows, or its products, continues to be used, living organisms will find entrance into the human organism. The bovine type of bacillus is responsible for about 1 per cent. of infection in man and 5 per cent. of infection in children under 15 years of age.

S. J. Wang and F. Cooley, during the last year and a half at Sea View Hospital, Staten Island, N. Y., examined the breast milk of

twenty-eight tuberculous women for tubercle bacilli. There was no apparent mammary disease or suspicion of such in any case. The specimens of milk were obtained from these women twice each week, from 3 to 5 c. c. being gathered by breast massage, under aseptic precautions, for each test. All specimens were examined within two hours after they were withdrawn from the breast. An ordinary smear was first stained for tubercle bacilli, then the remainder of the specimen was reduced with weak antiformin solution, and the resulting sediment was examined for tubercle bacilli. Specimens from each of the last fifteen of the series were injected into guinea-pigs intraperitoneally; the guinea-pigs were killed six weeks later and tuberculous changes sought.

All the specimens injected into guinea-pigs were negative. No tuberculous changes were found, and no effects of any kind from the milk injections occurred in the animals.

Altogether there were about 450 microscopic examinations of specimens taken bi-weekly from the whole series of twenty-eight cases. These were all negative except one, which the writers think was questionable.

Some observations were also made on two guinea-pigs that were fed breast milk from two tuberculous women. The milk from these women, both of whom had normal, full-term deliveries in the hospital, was fed to the animals three times a day for one month. As much milk as possible was obtained for each feeding, the amounts varying from 10 to 40 c.c. A small amount of lettuce and bread also was fed them. This experiment was carried out to ascertain whether the animals became tuberculous and, if they did not, whether they gained weight and thrive on these feedings. If these specimens of milk contained toxic substances, it was thought that the guinea-pigs might show some effects from the daily ingestion of such relatively large amounts. Both guinea-pigs had lost weight at the end of the thirty days. Soon after necropsy was performed on the guinea-pigs and no evidence of tuberculosis was found in either animal.

The authors feel that the negative results of these experiments seem to indicate that tubercle bacilli are infrequently found in the breast milk of tuberculous women who have no mammary disease. The possibility of infection from such milk is probably slight, but it is very likely best to inderdict nursing in every instance, because of the additional dangers, that of infection during the intimate relationship of the mother and the nursing child, the possibility of toxic substance in the milk, and the bad effects of nursing on the mother. An exception might be made in the instance of a mother with a closed case of tuberculosis, although it is often difficult to distinguish between a closed and open case after pregnancy and labor. The tuberculous

woman undergoes a profound strain before and during childbirth, and it frequently takes a long period of observation to ascertain whether her disease has been activated.

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For ten years H. Barbier¹³ has been interested in the question of tuberculosis in infants and has sought for this disease at all necropsies. One of his interns found a proportion of 32 per cent. of deaths from tuberculosis in infants under 2 years of age. Another statistical report showed tuberculosis in 39 per cent. of children dying from all causes. But Barbier thinks statistics furnished by necropsy reports are lower than those which represent the morbidity of tuberculosis in infants, for he thinks that all infants below 2 years inoculated with tuberculosis do not die, as is proved by finding among older children lesions which evidently originated at a very early date.

As to the frequency of ulcerative forms, the author found eighty-four cases at 194 necropsies, and adding these personal observations to those published by different authors, Barbier found in a total of 766 necropsies on tuberculous infants 220 cases of cavities, or 29 per cent. Cavities rarely form before the third month and they usually

occur between the sixth and eighteenth month. The frequency of these ulcerative lesions goes to prove the great morbidity of tuberculosis in infants, and Barbier thinks that often symptoms like dyspnea, febrile attacks and cough in so-called atrophic infants are but manifestations of the evolution of a tuberculosis.

M. S. Reuben¹⁴ reports a case of tuberculosis in a nine weeks old baby following ritual circumcision. On the eighth day the child had been circumcised by a mohel, who aspirated the wound by means of a glass tube. Within a week the wound of the circumcision had healed. Five weeks later the mother noticed a swelling in the right groin and brought the child to the writer for treatment. Physical examination showed that the inguinal glands in the right groin were enlarged, the mass being about the size of the small finger; there was also swelling of the left inguinal glands, but not to the same extent as on the right side. Examination of the penis revealed four small tuberculous masses on the anterior surface of the circumcision scar. On palpation of these masses one obtained the feeling not unlike that of shot under the skin; they felt hard and indurated. The largest of these tuberculous masses was excised and microscopic examination showed the tissue was infiltrated with numerous tubercles and diffuse tuberculous inflammatory material. The von Pirquet reaction of the infant was positive. The mohel was found to be suffering from advanced tuberculosis and his sputum was loaded with tubercle bacilli.

Reuben reviewed the literature on this subject and found reports of forty-two cases of tuberculous infection following circumcision. He thinks the incidence of this infection is much greater, as many cases have probably not been reported. The treatment is early excision of the tuberculous tissue of the penis and of the inguinal glands on both sides.

The rarity of Addison's disease among children makes a case reported by J. Comby¹⁵ of especial interest. The case was that of a 13 year old girl whose father had died of pulmonary tuberculosis eight years before. The necropsy showed old pleuritic adhesions, but no tubercles in the lungs or tracheo-bronchial glands. The right suprarenal capsule was much enlarged, nodular and softened. On section a caseous fluid escaped and it was impossible to distinguish any normal tissue. The kidney of the same side showed several yellow tubercles. The left suprarenal was enlarged, but less so than the right, and contained a number of tubercles. The liver and spleen were increased in size and also contained tubercles.

Commarata¹⁶ describes a case of tuberculous meningitis simulating multiple sclerosis in a 3 year old boy. Six months before consultation he developed a tremor of the right hand, which was worse during the

day. Three months later the boy walked with a tremulous, spastic gait and sensation was found to be lost in the right leg. There was an intention tremor so marked that he could not raise a glass to the lips. No evidence of meningitis was present and a diagnosis of multiple sclerosis was made. Some weeks later he was seized with fever, headache, vomiting, stiff neck and a convergent strabismus, which in a few days terminated in convulsions. Lumbar puncture gave a fluid under increased pressure containing tubercle bacilli. There was some temporary improvement after the puncture, but death occurred shortly.

J. Bonaba¹⁷ discusses three cases of tuberculoma of the cerebellum in children. He describes symptoms and gives the necropsy report in each case.

A. D'Espine and V. Demole¹⁸ report a case of tubercles of the pons in a 7 year old boy. From the symptoms a diagnosis was made of a tubercle in the eminentia teres of the right side of the pons. Necropsy showed tracheobronchitis, caseous pulmonary tuberculosis, caseated tracheobronchial glands, ulcerative intestinal tuberculosis, multiple conglomerate tubercles of the brain, cerebellum, and bulb, recent miliary tuberculosis and acute tuberculous meningitis. The findings in the pons were especially interesting. Two tubercles were situated in the right eminentia teres, one in the center of the pyramidal tract, which had almost destroyed the point of origin of the right oculomotor nerve and greatly injured the facial. This lesion explained the paralysis of these two nerves. The second tubercle was situated in the center of the right pyramidal bundle, but only separated the fibers and did not destroy them, a fact which explained the exaggerated reflexes and clonus and the absence of hemiplegia.

R. L. Ash¹⁹ reports an unusual case of tuberculoma of the spinal cord in a 19 months old baby, giving it as a contribution to the study and diagnosis of spinal tumors in childhood. The clinical diagnosis was intramedullary or extramedullary tumor of the spinal cord, compression myelitis and meningitis, probably of tuberculous origin. The child died and necropsy confirmed the diagnosis. There was a general tuberculosis, a tuberculoma of the cerebrum and a tuberculoma of the spinal cord. This latter was olive-shaped, 2.5 by 1.2 cm. in size, and was situated extramedullary in the cervical enlargement of the spinal cord. It was grayish-white and caseous in appearance and microscopically was composed of typical tuberculous tissue. Of special interest in this case is the fact that a tumor of the spinal meninges, which was diagnosed during life, was the first manifestation of a generalized tuberculosis in a child of 19 months. Xanthochromia with massive spontaneous coagulation and pleocytosis was an attending syndrome.

W. E. Ladd²⁰ discusses the subject of tuberculous cervical adenitis

in children. He says the commonest portal of entrance of the infection is the tonsil, though occasionally the adenoids, teeth, ear or skin of the face and scalp are the source, and that further investigation should be undertaken to give a more definite answer to the question of the disease originating from bovine or human type of tubercle bacillus. If it becomes firmly established that milk is responsible for the majority of infections, it would seem possible greatly to reduce their frequency by securing nontuberculous milk supplies.

F. Harbitz,²¹ since his last article in 1905, has investigated further the question of tuberculosis of the lymph nodes and has paid particular attention to the general form of the disease, its frequency in children and adults, its origin and its importance as a cause of death. He says that it is not well known that tuberculosis of the lymph nodes may be a general disease, that is, one which affects the entire lymphatic glandular system. It may be encountered incidentally in postmortem examinations or, as is more commonly the case, it may occur with extensive and, as a rule, eventually fatal cases of tuberculosis, when it is the older and primary lesion and thus indirectly the cause of death. The author's observations were based on 2,906 necropsies, 2,489 of adults and 417 of children. He divides tuberculosis of the lymph glands into seven groups, which include tuberculosis of the bronchial, cervical and abdominal glands, combinations of these three groups, and last and most important, general lymph gland tuberculosis. In this important group were included sixty-one cases, thirty-two of adults and twenty-nine of children. Of the cases in children twenty occurred during the first year of life and in almost all there was a history of tuberculosis in the immediate relatives, usually in the parents. In all these, extensive tuberculous processes were found in the internal organs, as well as in the glands, so that it was impossible to trace the connection between the two processes, but the process in the lymph nodes was clearly the most marked and oldest. The lymph nodes of the neck, of the thorax and of the abdomen were extensively affected, occasionally also those of the axillary and inguinal regions. The process in the neck was a descending one, most marked above and extending down to the supraclavicular space, where the glands were smallest. In the thorax the process was an ascending one, the glands were smallest above around the trachea, while around the bifurcation and pulmonary hilus they were largest. In the abdomen the tuberculosis was usually limited to the mesenteric nodes, or retroperitoneal nodes, where they formed large masses around the aorta, celiac axis or in the hilus of the liver or spleen. In general it did not appear that there was a continuous extension from one group of glands to another, but the impression was rather that a repeated infection had taken place by different paths,

especially as the process appeared to be of different ages, old in some glands, recent in others which had no direct connection with the first. This could be explained by exposure to infection at different times, both by inhalation and swallowing, and the possibility of reinfection was often established by obtaining a history of contact with a phthisical patient. As to the mode of extension, Harbitz thinks that after one or more infections of different groups there is extension along the lymph vessels and then a dissemination through the blood to all groups of glands, until it is impossible to trace the route or mode of infection. Pulmonary tuberculosis appears to be the cause of death in about one-half the cases of general lymph gland tuberculosis. Particularly in older children, but not rarely in the first years of childhood and in infancy, the tuberculosis in the lungs assumes the form of phthisis in adults with cavity formation. Less frequently there is an apical tuberculosis due to extension to the lungs from the nodes in the upper part of the mediastinum or supraclavicular regions. Tuberculosis of the intestinal tract is the cause of death in about one fourth of the cases. In these instances the primary lesion developed presumably in the abdominal lymph nodes. Miliary tuberculosis, or tuberculous meningitis is also the cause in about one fourth of the cases, especially in instances of tuberculosis of isolated groups of glands.

A. T. Jones²² reports nine cases of tuberculous glands of the mesentery, three in children. Operation was performed to relieve surgical symptoms and at the operation the primary cause of the trouble was found to be disease of the mesenteric glands. Jones believes that the tuberculous mesenteric gland is often a primary disease of the true tuberculous type, but the bovine type is undoubtedly present in many children without producing symptoms, the glands remaining quiescent or having a tendency to subside. As a rule, it is impossible to make a correct diagnosis before operation, unless there are glands which can be felt through the abdominal wall or by the finger in the rectum. There are two clinical types: (a) a slightly progressive one, generally with palpable glands; (b) an acute fulminating type, frequently simulating, and impossible to differentiate from, appendicitis. The prognosis in the subacute stage is good without operation. In the acute stage exploratory laparotomy should be performed, but the glands not removed, unless there are definite indications of adhesions or ulceration, or unless the large size of the mass produces much pain or obstruction. From Jones' experience tuberculous glands of the mesentery may present no symptoms until breaking down begins in the glands, and after that there are symptoms of tuberculous peritonitis, intestinal obstruction, or acute appendicitis. He says that in children and young adults with a history of right sided abdominal pain with or

without palpable masses, inflamed mesenteric glands should be considered a possibility.

C. M. Du Pan²³ describes an unusual case of tuberculosis of the mesentery in an 8 year old boy.

TUBERCULOSIS OF THE TRACHEOBRONCHIAL GLANDS

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C. Floyd, H. K. Boutwell and A. W. George²⁴ discuss the pathology, symptoms and diagnosis of enlarged thoracic glands, a term they prefer to bronchial glands, the one now in use, as it includes the groups of glands not only about the root of the lungs, but also on either side of the trachea. Enlargement of thoracic glands has been noted in many infections, not only in tuberculosis and Hodgkin's disease, but also in the acute contagious diseases of children, as measles, scarlet fever, pertussis, and still more recently in the common acute bronchial colds. Most observers, however, are of the opinion that tuberculosis is the most common cause of enlargement of these glands. The writers believe that the symptomatology of enlarged thoracic glands is still one of considerable uncertainty and obscurity. Lassitude, slight elevation of temperature, more or less constant thoracic pain, especially in the interscapular region, and a brassy cough are the symptoms most often noted. But the writers have failed to detect any constant symptoms in this condition. When, however, there occur persistent elevated temperature and pulse and harsh, dry cough, anemia and lack of normal development, without other explanatory condition, the possibility of thoracic adenitis should be considered. The diagnosis has given rise to a great variety of opinions as to the value of certain signs commonly associated with its presence. The most important ones are enlargement of the superficial thoracic veins, irregularity of the pupils, the so-called Eustace Smith sign, an increase in normal area of dullness, extending outward on either side of the sternum, D'Espine's sign, vertebral dullness or resistance, or both, below the first dorsal spine, which does not change with full inspiration. One or more of these signs, supplemented by positive evidence of fluoroscopic examination and roentgenograms, are generally considered pathognomonic of tracheobronchial adenitis.

The authors' observations have led them to believe that in children whose bronchial glands on the right side are considerably enlarged, there not infrequently occur at the right apex definite signs of consolidation, such as dulness, increased resistance, limited expansion and bronchovesicular breathing. Prolonged observation, clinical and by means of the roentgen ray, have shown in these cases no apical lesion and, with subsidence of the bronchial nodes, there is entire disappearance of these signs. The condition seems to be due to a retraction of the apex, together with a reflex limitation of its function. The authors think that no single sign should be depended on, but in the majority of instances, where parasternal or paravertebral dulness occurs, the diagnosis is correct. D'Espine's sign is of importance, but to a slighter degree than formerly thought. It may, however, be the first clinical sign to appear and may be the only one in acute respiratory infections. The other signs, while they occasionally occur in extensive involvement of the thoracic glands, are too infrequently present to be relied on. No study of bronchial or hilus region is complete without repeated roentgen ray examination, but even here the shadows present may be confused or accompany other conditions, and reliance should not be placed on roentgen-ray examination alone. The authors believe far too little stress has been laid on thoracic adenopathy and that with the advent of more exact methods of study of diseases of the chest the importance of enlarged thoracic glands will be recognized.

M. E. Lapham²⁸ divides the symptoms of tuberculosis of the bronchial glands in infants into those due to pressure and those due to absorption of the toxins. Death may occur if the caseating glands perforate the air passages and fill them with caseous material, or if the infectious material is carried to other parts of the lung and induces caseous or bronchopneumonia, acute miliary tuberculosis, typhobacillemia of Landouzy, or meningitis. The symptoms of pressure are due either to irritation of the pulmonary nerves lying on the surface of the trachea and bronchi or to obstruction to the passage of air. Symptoms suggestive of enlarged bronchial glands are high-pitched, explosive paroxysmal attacks of coughing or a cough resembling the bellowing of a young hound. Often the cough is the first and only symptom for a long time; again it is preceded or overshadowed by the expiratory dyspnea. The expiratory dyspnea is the most constant and reliable symptom of obstruction of the air passages. Frequently there is a bitonal cough, due to pressure on one recurrent nerve and lack of symmetrical functioning of the vocal cords. Vomiting may prove a distressing symptom. Bronchial râles are very common and characteristic.

Symptoms caused by absorption of the toxins are vague; the vaso-

motor, gastrointestinal and hematopoietic systems are chiefly affected. It is possible that the vasomotor system may show the first effect of the toxins, which cause a fall in blood pressure and relaxation of the vessel walls, resulting in sluggish circulation in the gastro-intestinal and hematopoietic systems. Spasmophilia and chorea, which frequently precede tuberculosis, may be manifestations of vasomotor disturbances. The functional activities of the gastro-intestinal tract may be stimulated or depressed by the tuberculotoxins. Hyperacidity is a result of overstimulation. The child regurgitates food, is restless and fretful, but does not lose appetite. Anacidity, on the other hand, causes lack of appetite, constipation and apathy. There is loss of weight and, finally, marked atrophy. There is, however, nothing specific or suggestive of tuberculosis in the disturbances of nutrition resulting from tuberculous toxemia. This is true also of the disturbances of the hematopoietic system. There is hardly a disease of this system, from simple chlorosis to pernicious anemia, which cannot be simulated by tuberculous toxemia.

Tuberculosis of the bronchial glands is not necessarily a wasting or cachectic disease. Fatal perforation and such consequences of perforation as meningitis occur invariably in well-nourished infants.

H. M. Rich²⁶ says the diagnosis of tuberculous bronchial glands is made by considering four groups of facts: (1) history of exposure; (2) presence of symptoms otherwise unexplained; (3) physical signs, including the roentgen-ray findings, and (4) the specific reaction to tuberculin.

An infant living in contact with an open case of tuberculosis practically never escapes infection. A history of exposure is strong predisposing evidence in favor of tuberculous infection having taken place. The symptoms are somewhat indefinite. The earliest symptom is the decline of customary activity, with increased irritability. Loss of appetite and failure to gain weight follow. Many times the writer has noted repeated fleeting attacks of pallor. The temperature range is but slightly disturbed. Cough may or may not be present. It is usually brassy, paroxysmal and ineffective. Change of voice, hoarseness, and attacks of paroxysmal dyspnea may be noted. In the early stage none of the usual signs of phthisis are observed. The findings point to increased mediastinal activity, shown by the presence of D'Espine's sign and of dullness on direct percussion over the vertebrae. A third sign is a variation in the intensity of inspiration in the lower interscapular spaces. It may be heard on either side and is usually quite marked. The findings should always be substantiated by roentgen-ray examination, by which the increased density of the mediastinum can be easily demonstrated. Specific reactions may be

obtained by the von Pirquet test for the first three years of life, by the Calmette test in later life, if no contraindications exist. A positive result with either test means an active tuberculous process. A negative test may be disregarded in the presence of other strong evidence of bronchial gland tuberculosis. The early stage of a mediastinal tumor is perhaps the most difficult condition to differentiate from bronchial gland tuberculosis. The symptoms and physical signs are at first the same, but gradually change as the tumor grows larger. More frequently, however, a distinction must be made between bronchial gland tuberculosis and convalescence from pneumonia. Physical signs of mediastinal density may persist after the signs in the lungs have cleared and fever and malaise may continue for a considerable period. A tuberculin test here is of considerable value. Measles followed by enlarged bronchial glands may also offer difficulty in differential diagnosis.

C. J. Bloom's²⁷ experience with D'Espine's sign covers a series of seventeen cases, in which the sign was positive and a diagnosis of enlarged tracheobronchial glands was made before the roentgen-ray examination. From his study, Bloom wishes to impress the following facts: In infancy the anteroposterior diameter of the chest is relatively small and the glands are normally enlarged, so alteration in their size can be detected and is an aid in diagnosis. D'Espine's sign is a valuable aid in the diagnosis of tracheobronchial tuberculosis, but a positive D'Espine sign only shows an enlargement and does not signify that it is due to a tuberculosis. The sign is most significant under 10 years of age.

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The following outline for the diagnosis of tuberculosis in children is formulated by J. A. Miller and B. H. Waters²⁸ for the National Association for the Study and Prevention of Tuberculosis.

In the history record should be made of exposure to infection (especially if prolonged), delayed convalescence from any illness, malnutrition, underweight or loss of weight, cough, expectoration, hemorrhage, pain, pleurisy, dyspnea, night sweats, digestive disturbances and ear discharge.

Important physical signs are persistent and persistently localized râles, additional abnormal signs elicited by the usual methods of examination, any gland, joint, bone, muscular, cutaneous, ocular or aural abnormalities. Essential for diagnosis of pulmonary tuberculosis are distinct persistent or persistently localized adventitious sounds in the chest. Temperature over 99 F. by mouth recorded twice a week for a month and not otherwise to be explained. A positive tuberculin test. Exceptionally, in the absence of adventitious signs, a diagnosis of tuberculosis can be made in the following instances: (1) A positive tuberculin reaction with an unquestioned and otherwise unexplained hemoptysis, with or without a positive roentgenogram; (2) a positive tuberculin reaction in children under 3 or 4 years of age without constitutional symptoms, and in older children with frequent cough or rapid pulse or fever, and a roentgenogram which shows unmistakable mottling in the pulmonic field. No patient with fever and persistent physical signs should be considered free from tuberculosis until the tuberculin test has given a negative reaction three successive times. Examiners are reminded that undue importance should not be ascribed to slight vocal and respiratory modifications or to slight alterations in the percussion note so frequently present in children, especially at the apices.

For the diagnosis of forms of tuberculosis other than pulmonary there must exist suggestive physical signs or constitutional symptoms or both, a negative Wassermann and a positive tuberculin test.

On a study of the case records of 200 children in a sanitarium for tuberculosis, H. D. Chadwick and R. Morgan²⁹ summarize the essentials in the diagnosis of this disease. They emphasize the importance of symptoms indicating tuberculin absorption, namely, weakness, undue fatigue, fever, poor appetite, failure to gain, or loss of weight

and nervous irritability. Symptoms of local involvement are cough, hoarseness and occasionally streaked sputum. The usual physical signs are dulness in the interscapular region radiating into the apexes at the back, frequently not elicited in front. There may or may not be changes in the respiratory sounds. Râles may or may not be present. Symptoms, both constitutional and local, together with a history of exposure, are to be given greater weight in making a diagnosis of active tuberculosis than the presence or absence of physical signs. Percussion is more important than auscultation. A thickened area in the lung or region of the bronchial glands does not in itself mean active tuberculosis. It may be a healed lesion that needs no treatment. Such thickening may also be caused by other diseases than tuberculosis. The child showing constitutional symptoms, even without local signs of disease in the chest, should be considered suspicious, kept under careful observation, and subjected to hygienic treatment in the home. Signs in the chest without constitutional symptoms indicate an old inactive infection that needs no treatment. Individualization and common sense must be used, all the factors in the case weighed and, with experience as a guide, few errors in diagnosis will be made.

M. Fishberg³⁰ discusses the diagnosis of pulmonary tuberculosis in children of school age. He believes it exceedingly rare at this age, and that when it does occur it is of the same type as in adults. Moreover, the physical findings and symptoms are practically the same as when the disease occurs in adults. Thus, children with pulmonary tuberculosis (if the disease is active) have cough, fever, night sweats, tachycardia, and emaciation. The cough may be mild or severe, may be paroxysmal or croupy, or not unlike whooping cough. The fever may be of any type, but it must not be forgotten that instability of temperature is very common and that fever alone is not to be considered pathognomonic of tuberculosis. Excitement, excessive exercise, or a slight gastric disturbance may elevate it. Also moderate elevation of temperature is very frequently due to focal infections of the nose and throat. Night sweats are only significant when they occur during the early morning hours. The pulse rate is an important diagnostic criterion. Active tuberculosis of the lungs may be excluded, when a child under 10 years has a pulse rate of less than eighty per minute. Tachycardia is almost invariably the rule in phthisis of children. Enlargement of the supraclavicular glands is also of great diagnostic significance. It is nearly always due to tuberculosis of the apex of the lung of the affected side. With any or all of the above symptoms pulmonary tuberculosis should be suspected, but no diagnosis made unless the lesion is localized by physical exploration of the chest. In pulmonary tuberculosis of children the lesion is almost invariably

localized at the apex, and statements made by some authors to the effect that it is found at the base or in the region of the hilus result from a confusion of disease of the tracheobronchial glands with disease of the pulmonary parenchyma. Pulmonary tuberculosis should be diagnosed in a child with lesions in the lower lobes, only when tubercle bacilli are found in the sputum, or when all other possible causes have been excluded. Bronchiectasis and multiple abscesses of the lung may give signs similar to those of tuberculosis. In many children suffering from adenoid vegetations of the nasopharynx there is impaired resonance in one of the apexes, usually the right, with bronchial or bronchovesicular breathing. Inasmuch as there is cough and often fever or loss of weight, the diagnosis of tuberculosis is likely to be made. Similar physical signs occur also in children with valvular heart disease. The roentgen ray is of immense value in diagnosis, if properly interpreted. In pulmonary tuberculosis in children the opacities will be found in the parenchyma of the apex, as in adults. Roentgen-ray findings, however, without constitutional symptoms do not justify a diagnosis of pulmonary tuberculosis. As regards the findings of tubercle bacilli in the sputum of children with pulmonary tuberculosis, Fishberg has found them in nearly all his cases. The tuberculin test he says is of no value in children over 4 years, as it only indicates tuberculous infection, not tuberculous disease.

In J. Signorelli's²¹ experience the physical signs were the most important factor in the diagnosis of pulmonary tuberculosis in children. Next was the roentgen-ray examination, which has never failed to corroborate a lesion found clinically, while in obscure cases it has often pointed the way to a conclusion. The von Pirquet test applied three consecutive times, he found, gave a positive reaction in 85 per cent. of children with tuberculosis, while children with nontuberculous lesions always failed to react. D'Espine's sign he found present in 80 per cent. of tuberculous and in 15 per cent. of nontuberculous patients. The finding of tubercle bacilli in the sputum was an absolutely indisputable sign. Signorelli emphasizes the importance of not depending on one mode of examination or on one single examination in making a diagnosis, even though it might appear conclusive.

A. Lankester²² has attempted to find some physical test, easy of application to schoolchildren on a large scale, which could be relied on to give an indication of the extent and prevalence of tuberculosis in the environment from which the children come. He thought that as a very large percentage of enlarged cervical glands are due to tuberculous infection, he might be able to determine a true correlation between the percentage of children showing enlargement of these glands and the number of cases of phthisis in the community to which

they belong. After compiling and studying statistics, however, he has come to the conclusion that the gland index method needs to be further safeguarded before it can be regarded as suitable for general adoption as a measure for tuberculous prevalence. The reasons for this conclusion are the element of possible variation due to a personal factor in the examiner, and to the fact that tuberculosis is only one among several causes of glandular enlargement.

J. H. Mason Knox, Jr.,⁴⁰ reports the results of a study of the von Pirquet cutaneous test for tuberculosis in a series of children on whom careful necropsies were performed. The test was made as a routine measure with Koch's old tuberculin. During the period of investigation, from November, 1912, to April, 1917, there were 2,940 children admitted to the hospital and there were 750 deaths. Necropsies were performed on 324 children. Two hundred and fifty-six, or 80 per cent., were found free of tuberculosis, and sixty-eight, or 20 per cent., were found to have tuberculous lesions. Of the 256 cases having no tuberculous lesion, the tuberculin test had been made in 172 instances and was negative without exception. Of the sixty-eight cases in which tuberculous lesions were found, the von Pirquet test had been performed in sixty-one. Of these it was positive in forty-five and negative in sixteen. The negative cases were carefully analyzed. In twelve instances the patients had a rapidly advancing, widespread miliary tuberculosis, in two instances a tuberculous meningitis, in two, advanced pulmonary tuberculosis, and in one, a tuberculous peritonitis. Knox concludes from these results that the cutaneous tuberculin test as described by von Pirquet is a most reliable aid in the detection of tuberculosis in children; that a positive reaction invariably indicates a tuberculous focus in the body, and that a persistently negative reaction establishes the fact that there is no lesion except in those extremely sick patients, where the presence of tuberculosis can be readily established by physical examination.

G. Lindberg³⁴ has applied repeated skin tuberculin tests to 129 children from 1 to 12 years in the hospital and sanatorium with which he is connected. The tuberculin skin test was applied to each arm and repeated after a week's interval. The reaction was measured in both the axial and transverse diameters twenty-four hours after the test and a week later. When neither diameter was over 5 mm. the reaction was recorded as negative. Of the 129 children, 33.3 per cent. showed a much more pronounced response to the second test than to the first. In 60 per cent. the response was weaker in the second than in the first; in 6.7 per cent. there was but slight difference.

Lindberg divides the patients into three groups—those with active, those with probable and those with nontuberculous lesions. Intensifi-

cation of the reaction, or positive sensitization, occurred in only 5.3 per cent. of the thirty-six cases in the first group; in 28.5 per cent. of sixteen in the probable group, and in 78 per cent. of the last group.

The results of the research testify that with inactive tuberculosis the response to the repetition of the tuberculin skin test is more pronounced than at the first test, while the reverse is the rule with active tuberculosis. The attenuation of the response to a second application of the test has thus a favorable instead of an unfavorable significance.

S. Pisani³⁵ reports his results with the cutaneous tuberculin test, when the injection is made in the skin over the affected viscera. In patients having unilateral renal tuberculosis without other active lesions he has observed that the cutaneous reaction is markedly positive in the lumbar region on the side corresponding to the affected kidney and negative on the other side. The reaction in the skin of the arm may be positive or negative.

In patients suffering from tuberculous peritonitis and in those with tuberculosis of the adnexa, the cutaneous reaction in the skin of the abdomen is very marked, while on the arm it is negative or only slightly positive.

In patients with incipient pulmonary tuberculosis, localized in the apex, with no fever the cutaneous reaction is more precocious and intense in the neighborhood of the affected part. The opposite is true with advanced lesions and in patients with high temperatures.

In patients with a bilateral pulmonary tuberculosis, recent or old, febrile or apyretic, the cutaneous reaction is more intense on the side of the less advanced lesion, a true paradoxical reaction.

In patients suffering from pulmonary tuberculosis with a therapeutic pneumothorax, the cutaneous reaction diminishes without becoming completely negative on the side of the pneumothorax; on the other hand, it becomes positive on the opposite side. If therapeutic intervention, however, has been performed early for a purely unilateral lesion, the reaction usually disappears on both sides.

In patients affected with pleurisy with effusion, the cutaneous reaction varies; usually the fluid hinders the manifestation of the cutaneous reaction.

Pisani concludes that the regional cutaneous reaction is merely a phenomenon of reaction in a region containing lymphatics which drain a tuberculous lesion. Its diagnostic significance is identical with that of the ordinary cutaneous reaction. Its essential characteristic is its greater sensitiveness.

H. J. Gauvain³⁶ applied the von Pirquet test with human and bovine tuberculin to children suffering from tuberculosis of the bones and joints. He wished to ascertain whether the reaction was constantly

present in this form of tuberculous disease; if not present, under what circumstances the reaction would not appear; whether it could be decided by using both human and bovine tuberculin for the test that the patient was suffering from tuberculosis of human or bovine origin; whether the degree of reaction would be an indication of the severity of the infection. The author employed Koch's old tuberculin prepared from the human type of bacilli, and his tuberculin prepared in the identical way from bacilli of bovine origin. The tuberculins were applied to suitable skin scarifications in dilutions of 1:64, 1:16, 1:14, and in full strength, each in approximately equal bulk and controlled by inoculation of the same quantity of sterile normal saline solution. In all, eighty cases were investigated. Local reactions to both human and bovine tuberculin were invariably present in patients from whom tubercle bacilli were isolated from the local lesions. The local reactions to human and bovine tuberculin, however, were found to be essentially similar. In twenty-three the reactions were so nearly equal that it was impossible to decide which was greater. In twenty-one cases the reaction to human tuberculin was somewhat greater than to bovine, and in twenty-five the reaction to bovine was slightly more marked than to human. In four cases the reaction to human tuberculin was markedly greater than to the bovine, and in seven the bovine was markedly greater than to the human. It was therefore impossible by the nature of the reaction to the tuberculin employed to differentiate the type of tubercle bacilli with which the patient was attacked. Gauvain found that patients who were weakly and cachectic, irrespective of the severity of the local tuberculous lesion, reacted feebly, while patients who were strong showed an intense or mild reaction, irrespective of the local lesion. No guide to prognosis could be found by comparing the reactions produced by the weaker and stronger solutions of tuberculin.

M. L. Brocq⁸⁷ reports an instance of lichen scrofulosorum developing around an intradermal tuberculin reaction. The patient, a 13½-year-old girl, entered the hospital April 19, 1917. For five years she had been frail and delicate and had suffered from enlarged cervical and submaxillary glands. During the last two years these had greatly enlarged, and, when the child entered the hospital, had formed voluminous masses on either side of the neck. There was also evidence of enlargement of the tracheobronchial glands. A month before entrance there had appeared on the anterior part of the thorax, the abdomen, in the hypogastric region on the lower part of the back, in the sacrolumbar region and in the region of the deltoids, lesions typical of lichen scrofulosorum. At the same time on the anterior surfaces of both legs were discrete, larger lesions, which were diagnosed as papu-

lonecrotic tuberculids. On entrance to the hospital an intradermal tuberculin test was made with one drop of a 1 to 10,000 solution of tuberculin. In forty-eight hours there was a strong local reaction and an elevation of temperature to 38 C. The center of the reaction was of an opaline tint, at least 1 cm. in diameter; the periphery was swollen and bright red. The following day there was a bulla in the center and two days later there formed a small superficial scab, which dropped off in fifteen days. Ten days after the formation of the scab there appeared around the intradermal reaction a bright red eruption having all the characteristics of a lichen scrofulosorum. Between the central scar and the eruption was a zone free of lesions, corresponding to the erythematous zone area which surrounded the central scar the first few days of the reaction. On the twenty-third of May a second intradermal reaction was made in the left thigh, which was followed by a reaction as strong as the first, although no eruption appeared. Following this second test the eruption on the arm seemed to fade. The two points to which the writer calls particular attention are the appearance of the lichen scrofulosorum around an intradermal tuberculin reaction and the development of a zone 2.5 cm. in diameter around the reaction where no eruption formed. He quotes several reports of eruptions following injection of tuberculin, but none which resembled this.

M. Kashara²⁸ believes he has discovered a specific diagnosis of tuberculous meningitis, by a focal reaction to tuberculin. After the removal of a certain quantity of cerebrospinal fluid by lumbar puncture for cytologic examination an intradural injection is made of from 0.01 to 0.002 mg. of Koch's old tuberculin diluted with 0.5 to 1 c.c. of physiologic salt solution. After six, twelve or twenty-four hours a cytologic examination is again made of the fluid, which is obtained by lumbar puncture, and a comparison made with that previously obtained. In this way the author examined nine cases and found that after the tuberculin injection there was an increase in the number of cells in general, and chiefly a remarkable appearance of red blood cells, a considerable increase in the lymphocytes, and a moderate increase in the polymorphonuclear cells. Moreover, in cases of tuberculous meningitis the cerebrospinal fluid after the injection is turbid and occasionally yellow in color. Kashara found no change in the cerebrospinal fluid after the injection of tuberculin in cases of epidemic meningitis and of chronic hydrocephalus.

J. Golay²⁹ has observed in the Children's Clinic at Geneva many cases of meningismus and of meningitis with a lymphocytosis which simulated tuberculous meningitis, and he has found that by a chemical examination a diagnosis can be made with more certainty than by a

cytologic examination, and more rapidly than by a bacteriologic examination. He emphasizes the importance of differentiating these conditions, especially in view of the benign character of meningismus and of the fatal outcome of tuberculous meningitis. Golay studied the spinal fluid in twenty-six cases of tuberculous meningitis and found in twenty-three a high albumin content, that is, ranging between 1 or 2 gm. per thousand, instead of the normal 0.1 or 0.2 gm. per thousand. In other forms of meningitis and meningismus it ranges between 0.1 and 0.3 gm. per thousand. For determining the amount of albumin the author used either the silver nitrate or neutral chromate of potassium test. Moreover, Golay found that the determination of the amount of chlorids was of great value in making the diagnosis. In the cases of tuberculous meningitis the chlorids ran very low. Instead of the normal 7.25 to 7.40 gm. per thousand they ranged between 5.5 to 6.5 gm., while in cases of meningismus and meningitis they remained within the normal limits.

J. Leffler⁴⁰ has made a study of the feces of 100 tuberculous children and has analyzed the literature on the finding of tubercle bacilli in the stools of children with tuberculous processes of the respiratory tract. Examination of the feces by the Reh method gave positive results in 16.4 per cent. of the cases, most of these being children of 11 to 14 years or infants under 1 year. The author believes that the examination of the feces should be undertaken as a routine procedure along with other diagnostic methods. He thinks it is especially valuable in infiltrating pulmonary tuberculosis of young children, where sputum containing tubercle bacilli is obtained only with difficulty, if at all.

PROGNOSIS

41. Hemplemann, T. C.: Prognosis of Tuberculosis in Infancy. *Am. Rev. of Tuberc.*, 1917, **1**, 99.

42. Hemplemann, T. C.: Frequency of Tuberculids in Infancy and Childhood and their Relation to Prognosis. *Arch. Pédat.*, 1917, **34**, 362.

43. Schwab, J. B.: The Diazo Reaction No Guide in the Prognosis of Tuberculosis in Children. *Nederl. Tijdschr. v. Geneesk.*, 1917, **1**, 1010.

In regard to the prognosis of tuberculosis in children, T. C. Hemplemann⁴¹ says that evidence is accumulating which proves that a certain number of children with pulmonary tuberculosis even in the first year of life do recover, and that this number could be increased if as much effort and care were expended on them as on those who contract it later. The author has studied the mortality of 130 cases of pulmonary tuberculosis in the first two years of life and has arranged the cases in three tables. Table 1 shows the number of children known to have died, the age at the time the diagnosis was made, and the interval elapsing between this and death. In this group

were sixty-four, of whom thirty-seven were less than 1 year old at the time of diagnosis, and twenty-seven were in the second year of life. Forty-six, or 72 per cent., died within three months after diagnosis. As many of these infants were brought to the hospital moribund, these figures give no reliable indication of the rate of progress of the disease. Eighteen infants lived at least three months after the diagnosis was made, nine lived over six months, seven over nine months, three more than a year, and one a year and a half.

Table 2 shows the number of children living at the time of the last note on the history sheet, their ages at the time of the diagnosis of tuberculosis and the length of time they were under observation. There were sixty-six cases in all. Thirty-one were followed less than six months, thirty-five more than six months. Thirty infants were observed for one year or longer, and some observed for periods of four to five years. Only two of these showed symptoms referable to the lungs when last seen, while seven gave other evidence of tuberculosis. Of these thirty, ten were under 1 year of age, when the diagnosis was made, and only one showed active tuberculosis at the time of this report. The other twenty infants were between the ages of 12 and 24 months when the diagnosis was made, and only one showed evidence of pulmonary disease at the time of the report, although six others showed other evidence of tuberculous disease.

Table 3 gives the mortality statistics of children who lived for at least one year. Under 1 year of age the mortality was 78.7 per cent.; from 1 to 2 years it was 57.4 per cent., and for 2 years, 68 per cent.

T. C. Hemplemann⁴² has made an effort to ascertain the relation of tuberculids to prognosis in children. Here and there in the literature he has found the statement that tuberculids are of very grave prognostic import in the tuberculosis of childhood, and that their presence is an indication of general miliary tuberculosis. Hemplemann's material consisted of 130 cases of pulmonary tuberculosis in infants under 2 years of age, thirty of whom showed papulonecrotic tuberculids, and ten cases of tuberculids in children between 2 and 12 years. In all but one of the forty cases there was evidence of lung or tracheobronchial lymph node involvement in addition to the tuberculids. Of the forty children, thirteen are known to have died, eleven of these being in the first year of life and the other two in the second. Eleven children were observed for a period of at least one year after the occurrence of the tuberculids and were doing well when last heard from. Five of these were in the first year of life, five in the second, and one in the fourth. Of the five under 1 year, three were observed for two years or longer, two for three or longer, and one for five years. Of the five in the second year of life, two were observed for three

years and one for four years. One other child, $3\frac{1}{2}$ years old when the tuberculids were discovered, was living at the time of the last note on the history, over two years later. In addition to these children there were sixteen more living, but they were observed for less than a year, and are classified in a separate group because of the uncertainty of their fate. From these statistics the author concludes that tuberculids bear no direct relation to prognosis, as some of the children under observation had showed tuberculids four or five years.

J. B. Schwab⁴⁴ comments on the difficulty of deciding the prognosis of tuberculosis in children. She studied the diazo and urochromogen reactions in the urine to see whether any light could be thrown on the subject. The children studied were under observation for various periods of time, some only a few days, others as long as seven years. Among them there were 23 with tuberculous meningitis; 15 with generalized tuberculosis; 5 with pulmonary and peritoneal tuberculosis; 10 with tuberculous peritonitis; 33 with pulmonary tuberculosis, and a number with tuberculous pleurisy and glands. The diazo reaction was constantly negative in 55, including 35 progressive and fatal cases, and constantly positive in 27, of which 23 have since proved fatal. The urochromogen reaction ran parallel to the diazo with a few exceptions and did not seem more sensitive than the latter. In 7 cases the diazo varied from positive to negative and clinically the prognosis in this group was always dubious or grave. In short, the article may be summarized by the statement that the diazo reaction is not a reliable guide for the prognosis of tuberculosis in children.

PROPHYLAXIS

44. Combe: Prophylaxis and Prevention of Generalization of Tuberculosis in Infants. *Le Nourrisson*, 1916, **4**, 347.

45. Moor, F. C.: Tuberculous Disease of Children. *Southern Med. Jour.*, 1917, **10**, 300.

46. Kirkwood, R. M.: The Child and the Tuberculosis Problem. *Pediatrics*, 1917, **29**, 46.

47. Kerr, J.: Phthisis and School Children. *Pediatrics*, 1917, **29**, 184.

48. Quimby, J. P.: The Preventorium for Children at Farmington, New Jersey. *Modern Hosp.*, 1917, **8**, 177.

Minor, C. L.: Importance of Control of Childhood Infection in the Crusade for the Eradication of Tuberculosis. *Southern Med. Jour.*, 1917, **10**, 122.

Combe⁴⁴ discusses at length the prophylaxis of tuberculosis in infancy. He says that infection during the first 18 months means death within six or eight months, and so must be prevented at any cost. Prophylactic measures include prevention of infection both by the bovine and human bacillus. To prevent bovine infection milk must be obtained from healthy, tuberculin-tested cows; otherwise it must be boiled or pasteurized. The greatest danger to the infant comes

from human infection — from some tuberculous member of the family — and measures to prevent this kind of infection are expensive and difficult to carry out in the homes of the poor and middle class, since the child must be kept from contact with the tuberculous individual and with objects contaminated by the bacilli. Phthisical mothers are the chief source of infection. They must not nurse their infants, not only because of the toxins the milk contains, but because of the great danger of multiple reinfection from the intimate contact of mother and babe. Tuberculous parents should never kiss their infants, and should limit contact to strict necessity, and that never without washing and disinfecting their hands. They should disinfect their mouths many times a day and hold a handkerchief before the mouth when talking, coughing or sneezing. To prevent infection from contaminated objects, all toilet and table articles should be boiled regularly after use. Soiled linen and clothes should be thrown into boiling water and pressed with a very hot iron. Floors should never be swept, but dusted with a cloth dipped in turpentine. Walls and floors should be washed frequently with antiseptics. The infant should never be allowed to crawl on the floor, or only on a freshly laundered sheet in a railed space. All toys, rubber nipples, etc., should be boiled each time they are given to the child. For the most part prophylaxis in the home is inapplicable and not efficacious and resort must be had to removal of either the patient or the infant. The author is of the opinion that the only means of preventing tuberculosis in infants is to found asylums where infants of tuberculous parents can be placed directly after birth. In France, Germany and Switzerland institutions of this kind are already established.

In case the infant has become infected, prophylactic measures must be taken to prevent generalization of the disease. This can best be done by increasing the resistance of the infant, by change of climate, by proper diet and heliotherapy. The author prefers subalpine to alpine climates for these infants and is not quite sure of the advisability of sending them to the seashore. He thinks heliotherapy is a great aid in raising the resistance, and uses not only sun baths but artificial rays (actinic), declaring the results with the artificial ultra-violet rays to be identical with those obtained with the sun's rays. As to diet, he believes that a great many tuberculous infants suffer from a toxic dyspepsia, with inability to digest fats, so they should be fed a fat-free milk to which has been added malt, farina and Soxhlet's sugar. In some instances they thrive better on albumin milk. A wet-nurse should be procured if possible.

In a paper on tuberculous disease of children, F. C. Moor⁴⁵ discusses first the frequency, the symptoms and the signs of the disease

and then emphasizes the importance of prophylaxis. He says the first decade of life is the period of greatest susceptibility to the infection, and the prophylaxis of tuberculosis in childhood is the most important proposition confronting the medical profession. Moor thinks the first requisite for the proper institution of preventive measures is a complete census of cases of tuberculosis and the enforcing of a law that all new cases be reported. In connection with these reports there should be collected data as to the home conditions of the patients, the number of rooms available for occupancy, the size of the family, and especially the number and ages of the children. These data should be arranged on a unit basis, and with such an arrangement one district nurse to each unit could make the rounds often enough to keep in touch with conditions in each family and to a certain extent combine the duties of a visiting tuberculosis nurse and child welfare worker. Other points to be emphasized are ample protection of all children under 5 and prevention of massive infection, which is sure to occur when there is active disease in either parents or some other member of the household. In families in which ignorance and poverty or a bedridden mother makes home conditions hopeless, there is nothing to be considered but the removal of the younger children to a preventorium, the establishment of which is one of the first problems.

A second and less important requirement in preventing infection is the control of bovine tuberculosis. This can be done by uniform state laws or, better still, by federal laws.

In addition, the author touches on the importance of improving the general physical condition of the child, especially during school age, and he suggests a school medical adviser as well as a school medical inspector. Every child who is anemic, under weight, scrofulous, or otherwise below par should be given the advantage of open air schools and receive especial care from the medical supervisor.

To the end of preventing tuberculosis in the child, R. M. Kirkwood⁴⁶ suggests a number of measures. Very important is the establishment in existing sanatoriums of maternity departments properly equipped and in charge of competent obstetricians, or the establishment of especial maternity sanatoriums or open-air pavillions in existing maternity hospitals, where pregnant women approaching term can be cared for under ideal conditions for a pulmonary invalid; where they can be delivered by a technic most careful to conserve strength, and where the new-born babe can be immediately removed from the tuberculous mother and fed by a nontuberculous wetnurse or by artificial means.

Other measures suggested by the author are the examination for tuberculosis of midwives, obstetric nurses and nurse maids; the sys-

tematic performance of the von Pirquet test on all children; the establishment of preventoriums for children in the pretuberculous stage; the passing of laws prohibiting the marriage of the tuberculous; careful hygiene of homes and schools; proper feeding of children; instruction of school teachers in regard to facts about tuberculosis and its prevention.

According to J. Kerr,⁴⁷ statistics in England show that in the five years before school age and in the years after school age the mortality rate from phthisis among females is continually decreasing, as compared with that of males, while at school age the mortality among boys goes down progressively faster than among girls. Similar statistics have been collected on the continent. The writer thinks this difference in the phthisis mortality between the two sexes represents a difference in vitality and preventable illness, and he emphasizes the necessity of a more natural life for both boys and girls, instead of the cloistered life of the old schoolroom.

J. Palmer Quimby⁴⁸ describes the Tuberculosis Preventorium for Children at Farmingdale, New Jersey. He says that this institution was organized primarily for the care of poorly nourished, underfed children, exposed to tuberculous infection in their homes, who had already contracted tuberculosis, as a positive tuberculin reaction showed, but who had no open lesion. At the preventorium over 100 children are accommodated. They are kept for an average period of four and a half months, so that the institution provides annually for nearly 600 children. In addition to a reception pavilion where all children are quarantined for three weeks in order to prevent infection of the large group, there are four open air shacks, each accommodating thirty-two children, a small infirmary, school buildings, a large administration building, with a dining room which seats all of the children, and, last but not least, 170 acres of land in the sandy pine belt, over which the children roam and play. As children are accepted between the ages of four and fourteen years, it is necessary to give school instruction. There are three teachers, and the two-hour school period provided has proved sufficient to keep the children up to their public school grades.

During the stay of the children at the preventorium the condition of their homes is looked into and improvements instigated. Every six months after discharge the children are visited in their homes and their physical condition and the surroundings noted.

The executive committee of the preventorium determined to help the general tuberculosis campaign by giving employment to tuberculous patients with arrested disease. At the time of writing this article there were fifteen people of this class there and the plan as a whole has proved successful. Also in connection with the preventorium there

has been built a nursery for the care of infants under 2 years of age of tuberculous mothers. Infants remain in the institution for a period of one year, practically living in the open air, and their resisting power is materially increased.

TREATMENT

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Combe⁴⁹ believes that tuberculin therapy is only justified in (1) children afflicted with closed tuberculosis or with limited lesions producing a minimum amount of tuberculin; (2) children who produce an insufficient quantity of antibodies, as those with tracheobronchial tuberculosis, and (3) infants whose organisms are not yet adapted to the formation of antibodies. As regards administering the tuberculin, Combe tried the subcutaneous method, but has discarded it because of disastrous results; but he has been very successful with the intercutaneous method. He begins the treatment with an intercutaneous injection of 0.01 mg. of old tuberculin. If the reaction following this amount is less than 5 mm. in diameter, he uses it for the initial therapeutic dose. If the reaction is larger, he commences with 0.002 or 0.001 mg. The injections are given twice a week and the dose doubled at each injection, if conditions warrant. The increase, however, is gaged by the local reaction and the behavior of the eosinophil cells. Progressive diminution in size of the local reaction, as the therapeutic dose of tuberculin is increased, indicates that antibodies are being produced and immunity established, and speaks favorably for the treatment. On the other hand, if the local reaction increases as the dose of tuberculin is increased, the treatment is harmful and should be discontinued. Moreover, in favorable cases there is an increase in the eosinophil cells, which begins two hours after treatment and lasts until the tuberculin is decomposed, so that forty-eight hours after the injection the count becomes normal again. If too large a dose of tuberculin

has been injected, the eosinophilia persists several days, until all the tuberculin is decomposed.

In ten years of experience the author has become convinced of the value of this method, and he has never known an accident to follow the injections. If begun while the disease is still localized, the temperature drops, the appetite improves, the patient takes on weight, and the course, often fatally progressive, is arrested. The method is of no value if the disease has become generalized.

Combe has lately used another agent with apparent success in the treatment of tuberculosis of infants, namely, roentgenography. In the year he treated fifty children suffering from glandular and pulmonary tuberculosis and observed an improvement in their general condition and in the pulmonary lesions as shown by the roentgenograms. The roentgen ray stimulates the formation of connective tissue around the tuberculous lesions. This was proved in one patient who came to necropsy. The child had a tuberculous peritonitis and a lesion in the apex of the lung. The apical lesion had been exposed to the roentgen ray three times at intervals of eight days, and at necropsy it was found arrested and walled in with connective tissue. The thymus gland was found atrophied, and if this was the result of the treatment a word of warning must be sounded, as early atrophy of gland may result in retardation of development.

N. R. Blumenau⁵⁰ believes that pretuberculous children should be treated with inunctions of tuberculin. He reports experiments on guinea-pigs which apparently prove that toxins rubbed into the uninjured skin, after it has been shaved and cleansed of grease, pass through the skin as through a special filter and induce the production of antibodies in the organism. The animals kept well and even increased in weight, although they were given inunctions of diphtheria toxin in a 50 per cent. ointment. They then survived the subcutaneous injection of four times the fatal dose of diphtheria toxin. The author's experiments on animals were not numerous, but the results were so convincing that he applied the method at once to seventy children. The most effectual technic was to apply a drop of pure tuberculin to the forearm and then shave off a scrap of skin through it. The mixture of the superficial layer of the epidermis and the tuberculin formed a thin salve-like mixture, which was then rubbed into the skin until dry. Adhesive plaster was applied over the spot. When this was removed twenty-four or forty-eight hours later, the skin underneath displayed a strong, or weak reaction, and the inunction was repeated after an interval corresponding to the strength of the reaction. The dose of tuberculin was also progressively increased to a total of four drops. At first the intervals were usually three or five days, but, when the 4-drop dose was reached, the intervals were a week. The results in

the cases of well defined tuberculosis, especially of the lungs, were, as might be expected, scarcely amenable to treatment, but in incipient or occult tuberculosis the therapeutic results were prompt and striking. Blumenau gives a brief summary of eighteen cases. Some of the children were 9 or 10 months old, but the majority were between 2 and 11 years. Parents usually brought the children to the dispensary because of lassitude, drowsiness and apathy, or the reverse, excessive nervousness and irritability. There was frequently loss of appetite, restless sleep, persistent headache, palpitation, cough, pain in the side or chest and in the bones of the arms and legs. The majority were frail and undernourished. In order to arrive at a diagnosis it is not sufficient only to examine the child, but careful inquiry must be made as to the health of the parents and other relatives to ascertain whether any of them may have had pleurisy or chronic pulmonary disease, or whether any child in the family may have died of meningitis, or any one in the building had a chronic cough. None of the symptoms described are pathognomonic of tuberculosis, but when a possible source of infection is known, Blumenau thinks the tuberculin test will often reveal that they are the results of autointoxication from some tuberculous focus.

J. Hollos⁵¹ emphasizes the importance of detecting latent tuberculosis in children, because he believes that with specific treatment it is in that stage completely curable in a comparatively short time. The symptoms of latent tuberculosis are the result of the toxins on various organs. Especially developmental defects are the result of this tuberculous toxemia. A child who has previously developed normally grows thin and pale, the skin loses its elasticity, the muscles become flabby, the bones are inclined to soften and bend. Digestive disturbances and loss of appetite develop. The child becomes nervous and excitable. He cries easily or is always sleepy. Tuberculous toxins either excite or inhibit the functions of the thyroid gland, so that there may be, on the one hand, vasomotor excitability, rapid pulse, tendency to sweating, and, on the other, stunted growth and mental backwardness. Vasomotor disturbances are very common in children with latent tuberculosis. There is headache, dizziness, irregular pulse, pallor or flushing of the face, cold hands and feet. These children catch cold easily, frequently have eczema and pruritus, pains in the muscles, joints or abdomen. Mental development, however, is usually unaffected. The tuberculous toxins also depress or excite the sexual organs, so that a latent tuberculosis at puberty gives a varied picture. Sometimes there is an early sexual development with profuse menstruation, dysmenorrhea, headache and palpitation. Sometimes menstruation is retarded until the sixteenth or eighteenth year, and then is scant and intermittent. The child grows rapidly but remains pale and weak, and

finally develops the characteristic tuberculous habitus. In boys early and repeated pollutions and sexual nervousness should arouse the suspicion of tuberculosis.

Childhood is the most favorable time to effect a cure of tuberculosis. The process is comparatively recent, retrograde changes and mixed infections have not occurred and lowered the vitality of the organism. Treatment must include (1) prevention of repeated infections; (2) establishment of increased resistance; (3) specific treatment. Under the present social upheaval it is almost impossible to improve social or hygienic conditions and so fulfill the first two requirements. All the more important is the specific treatment, which, according to Hollos, is a positive cure even in poor hygienic surroundings. He regards every infant and every child who lives in a tuberculous environment as infected and advises a course of tuberculin treatment. After eight years' experience with Spengler's I. K. (immune bodies) he is even more satisfied with the results obtained in the treatment of tuberculosis in children than in adults, and not only in latent cases, but in advanced and seemingly hopeless ones. But he has obtained the most beneficial effects from the I. K. in children who have no manifest lesion, only subjective and functional disturbances. Moreover, in these cases the I. K. is a great diagnostic aid, for improvement after injection of small doses (vi to vii dilutions) or after inunctions of medium strength (1:20,000, 1:40,000) establishes their tuberculous nature. A few months' treatment brings about a complete cure. Although individualization in treatment is necessary and close watching is advantageous, Hollos has been able to obtain results by giving injections every three or six weeks and depending on the patient's family to use the inunctions every two or three days. He thinks there is no contraindication for the use of I. K. in the treatment of tuberculosis.

C. Lassarre⁵² describes the heliomarine treatment of tuberculosis in children at the Wallenstein foundation. He thinks the wonderful climate of Arcachon associated with heliotherapy is a remarkable therapeutic combination. The foundation has two buildings, the sanatorium and the open air pavilion. The sanatorium is built 500 meters from the water's edge and accommodates forty patients. It has two operating rooms, hydrotherapeutic room, and means for complete radiosopic examination. The open air pavilion has forty beds, twenty for boys between the ages of 4 and 12 years, and twenty for girls between 4 and 18. It is located at the water's edge and is surrounded with pine woods. The routine of treatment is as follows: The children sleep eleven hours, are dressed and exercise in the sand until 8 o'clock, when they have their first meal, of milk or vegetable soup and stew. This is followed by the sun cure and the method of exposure is

practically the same as that of Rollier. At 10 o'clock there are gymnastics; at 11:30 rest in the open air for five hours, interrupted by the midday meal. The evening meal is at 6:30 and consists chiefly of farinaceous foods. Lassarre thinks that the sea baths are an important factor in the treatment. The first bath is given eight or ten days after the child's arrival and they are continued until December, when they are replaced by tepid sprays.

The physiologic effect of the treatment was studied on seventy patients. The pulse is accelerated but always remains full and strong. The blood pressure is diminished during exposure but becomes normal after the treatment. The respiration slightly accelerated. The weight curve always increases. As to the general therapeutic action, the children arrive pale, emaciated and asthenic, and in two months they are completely transformed. The appetite returns, the skin becomes pink, and the children are happy and contented. As regards the local effect of the treatment, the author's experience confirms the opinion of other observers that all local tuberculous lesions are favorably influenced by heliotherapy.

C. L. Hyde and H. L. Grasso⁵⁸ describe the Adams Memorial Hospital and the results of the Rollier treatment of tuberculosis obtained there. The plant consists of two pavilions one story high with terraces on all sides 21 feet wide, 12 feet covered and 9 feet uncovered. Each pavilion has a central administration building with a kitchen and dining room in the rear and a wing on either side containing two large wards and four private rooms. For the education of the children two teachers are assigned from the school department. There is a large open air school room used for certain class work and when the weather is inclement. The success of treatment has exceeded the writers' expectation. The effect on the general condition of the patient is most remarkable. There is a rapid disappearance of pain, fever and chills; there is a return of appetite and an increase in body weight and strength and an improvement in the blood conditions. The most characteristic local result in the treatment of tuberculous joints by heliotherapy is the return of motion. There is separation and painless spontaneous expulsion of sequestra and intense recalcification. Sinuses and ulcers discharge more freely at first, sloughing follows and the formation of healthy granulations, and finally, healing. Abscesses are often completely absorbed, as are effusions into the joints, peritoneum and pleurae. Up to date ninety patients have been discharged and there are at present 150 under treatment. The average length of stay at the hospital of all patients discharged was 8.4 months, while the average length of stay for those discharged as apparently recovered was 13.5 months. Of the patients who stayed three months or longer, 67 per cent. were discharged apparently cured or with the disease arrested.

Of those who remained six months or longer, 77 per cent. were discharged apparently recovered, and of those who remained nine months or longer, 82 per cent. were discharged apparently recovered. This shows the importance the length of stay has on the results in surgical tuberculosis. As far as the authors have been able to ascertain, there has been no recurrence of the disease in patients apparently recovered at the time of discharge.

W. G. White, A. E. Stewart and P. F. Shuey⁵⁴ describe the new children's building of the Tuberculosis League of Pittsburgh. As one of the chief functions of the Tuberculosis League is teaching undergraduate medical students and nurses, it was necessary to house in this one building many phases of the work. On the ground floor is a ward for fourteen girls and on the second floor a similar ward for boys. On the subbasement floor are the open-air school and toilet rooms, while dining and sewing rooms are on the floor above this. On the dining room floor are the roentgen-ray department and four isolation rooms. On the ground floor with the girls' ward is a small complete operating department, also a students' laboratory, while on the boys' floor is another isolation unit.

P. Tilli⁵⁵ reinjected subcutaneously the cerebrospinal fluid obtained by lumbar puncture in three cases of tuberculous meningitis, in children 3 months, 18 months, and 8 years old. In the youngest child the disease subsided and there was an interval of health, but the meningitis returned ten months later and proved fatal. The 8-year-old child recovered and has had no return of the trouble during the three years to date, but the meningitis has caused blindness and the head is much enlarged. The other child recovered completely under the subcutaneous injections of 1, 2 and 3 c.c. of spinal fluid injected every third day. The cure was complete and has been permanent during the two years to date. This is the only case, however, in which no bacteriologic tests were made.

P. E. Weil and Loiseleur,⁵⁶ with apparently good results, tried the injection of air into the pericardial sac in a case of pericarditis with effusion. The patient was a boy of 14 years, who in March, 1915, had had an infection called grip, complicated with bronchopneumonia and cardiac weakness. There had been edema of the lower extremities, cyanosis, enlargement of the liver, and ascites. When the writers saw the patient in June, they found signs of pericarditis with effusion and of cardiotuberculous cirrhosis, and a generally precarious condition. On June 2 a pericardial puncture was made and a liter of hemorrhagic fluid withdrawn. This was followed by temporary amelioration of the general condition. On July 11 a second puncture was made, 900 c.c. of seropurulent fluid removed and replaced by 500 c.c. of air. All symptoms quickly disappeared. Again, on the 19th, after the

removal of 300 c.c. of fluid, 300 c.c. of air were injected. The radioscopic examination then showed that the pericarditis had cleared up, but at the upper part of the right border of the heart was a pocket of pus. So a fourth puncture was made under control of the screen and 40 c.c. of fluid withdrawn and the same amount of air injected. On July 26 the child was doing well, had no fever since the second puncture, and could sleep lying down; the pulse was 120, of good quality and the respirations were 32. On August 3 another puncture was made and 300 c.c. of yellow fluid withdrawn and the same quantity of air injected. Then, for an entire month the general condition improved and the fluid did not return. On September 5, however, it was again abundant and a sixth puncture was decided on, when 800 c.c. of fluid were removed and 400 c.c. of air injected. On October 25, in spite of the general good condition of the child, the fluid reappeared, and 750 c.c. of fluid were removed and the same amount of air injected.

The authors insist on the advantage of this method of treatment, which is not painful and does not cause dyspnea or discomfort. The operation is not difficult when the effusion is large, and though very difficult when it is small, it can be performed under fluoroscopic examination with comparative ease. These advantages make it preferable to any surgical procedure for pericarditis with effusion.

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FAMILIAL SPLENOMEGALY

A CLINICAL STUDY *

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During the last year we had the opportunity to observe at least two cases which presented the clinical picture of splenomegaly of Gaucher's type. The family history runs as follows:

CASE 1.—The first child of the family, a boy, 2 years of age, was taken into the hospital in 1901; death soon occurred. To our regret, no clinical history was at our disposal, but the diagnosis, "hepatitis," made at that time, gives us reason to believe that the child had an enlarged liver.

CASE 2.—The second child, a brunette, 11 years of age, was admitted to the hospital for the first time in 1912. The skin, slightly yellow tinted, did not show any signs of marked jaundice. The spleen, distinctly enlarged, was hard and smooth, not painful on palpation; the liver was enlarged, especially the left lobe felt remarkably firm; no ascites; the urine contained small traces of urobilin. The white cell formula was normal. Both the reactions of Wassermann and von Pirquet were negative; no visible glandular enlargement; temperature practically normal.

A year later the same child was admitted for the second time. Although she had had no special complaints during the course of the year, she did not look as well as before. The size of spleen and liver had increased. The spleen extended to the navel; the left hepatic lobe was felt 5 inches below the ensiform cartilage of the sternum; no ascites, no jaundice. The urine contained no bile pigment, but showed a marked urobilin reaction; hemoglobin 70 per cent. (Sahli); blood count, 5,200,000 red cells, 6,800 white cells. Differential count: 64 per cent. neutrophils, 13 per cent. eosinophils, 0.3 per cent. basophils, 16.6 per cent. lymphocytes, 5.3 per cent. transitional cells. (The average blood count of a girl 12 years of age is 80 per cent. hemoglobin, 5,196,450 red cells, 8,555 white cells, polynuclear neutrophils, 53.79 per cent., eosinophils, 3.57 per cent., lymphocytes, 33.25 per cent., transitional cells 9.39 per cent.) There were slight anisocytosis and poikilocytosis. Both Wassermann and von Pirquet reactions were negative. There was no glandular swelling. The temperature was normal. Five weeks later sudden death occurred within a few hours after a serious hematemesis.

CASE 3.—Seventeen days after birth the third child died from an umbilical infection.

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CASE 4.—The fourth child, a boy, aged 11 years, dark blonde, looked healthy. The spleen was palpable beneath the costal margin; the urine showed a trace of albumin and urobilin.

Blood examination: hemoglobin (Sahli) 85 per cent.; red cells 4,280,000; white cells 8,850; differential count: polynuclear neutrophils 43 per cent.; eosinophils 8.7 per cent.; basophils 1.3 per cent.; lymphocytes 44 per cent.; transitional cells 3.6 per cent.; Türk's cells 1 per cent. Von Pirquet's test (human tuberculin), slightly positive; with bovine tuberculin, strongly positive.

CASE 5.—The fifth child was a girl, blonde, 9 years of age. Liver and spleen were not palpable; urine normal. Blood count: hemoglobin 87 per cent.; red cells 5,700,000; white cells 8,825; polynuclear neutrophils 40.5 per cent.; eosinophils 7 per cent.; basophils 0.7 per cent.; lymphocytes 48.5 per cent.; transitional cells 3 per cent.; Türk's cells 0.2 per cent. Von Pirquet's test was negative.

CASE 6.—The sixth child, taken into the hospital in May, 1916, a girl, 7½ years of age, brunette, did not look well. The abdomen was distended, with dilated veins; circumference on the line of the navel, 60 cm.; linea alba pigmented; no cutaneous hemorrhages; no bleeding from the gums; micropolyadenia; knee reflex and cubital reflex somewhat increased; bones not painful on percussion; second pulmonary sound somewhat accentuated; no pulmonary changes.

The spleen was distinctly enlarged; had a smooth surface; felt firm. The incisure was easily felt. The lower border of the spleen was felt 1½ inches above the anterior superior iliac spine; the right border was 2½ inches removed from the median line. The enlargement of the liver was located chiefly in the left lobe, firm on palpation, extending 3 inches below the costal margin, reaching almost to the spleen. The edge of the left hepatic lobe was sharp, of the right lobe dull; the right lobe felt soft. The incisure for the gallbladder was easily palpable; no ascites, no jaundice. The urine contained no albumin, no sugar, not more than physiologic traces of urobilin; the diazo test was negative; no bile pigment. Microscopically, there were a few chromocytes and leukocytes. The urobilin test was made quite frequently, with the result as stated, before the operation took place. The Wassermann test was negative; von Pirquet positive (strongly positive with bovine tuberculin, slightly positive with human tuberculin). The temperature was sometimes slightly elevated. The blood count always showed a leukopenia, varying from 3,000 to 6,200 leukocytes. Notwithstanding the leukopenia the number of mononuclear lymphocytes remained, on some days, normal or only slightly subnormal; no marked anemia. The amount of hemoglobin and the number of erythrocytes were practically normal (Table 1). Spleen and liver became slightly enlarged during the two months which the patient spent in the hospital before the operation; splenectomy was performed on July 18.

CASE 7.—The seventh child was admitted to the hospital in May, 1916. The patient was a girl, 5½ years of age, looking well, well nourished, of the brunette type, but not so dark as her little sister. The injection of the mucous membranes was satisfactory. There was pigmentation of the linea alba and a few pigmented small spots on the skin of the abdomen, but no jaundice. The reflexes were not increased; a slight micropolyadenia existed; no heart murmurs; at the base of the left lung there was slightly impaired resonance on percussion, an inch wide, without auscultatory changes. The circumference of the abdomen on the line of the navel was 53 cm.; dilated veins were slightly visible; no free fluid in the abdominal cavity.

The spleen was hard; its surface smooth, not painful on palpation; the incisure was not clearly felt. The spleen extended 1 inch above the superior anterior iliac spine; the right edge was 2½ inches removed from the navel. Splenic dullness was heard in the axillary line at the ninth rib. The hepatic enlargement was chiefly located in the left lobe, although not so marked as in

the previous case. The surface was smooth, not painful on palpation. The lower border of the liver was felt in the median line, 4 inches below the ensiform cartilage. The hepatic incisure was distinctly palpable. In the anterior axillary line the hepatic border was felt 2 inches below the costal margin. The urine contained no albumin, no sugar, no bile pigment. The repeated urobilin test showed only once a slightly increased amount of urobilin. Wassermann's test was negative; von Pirquet's test was positive (more marked when using bovine tuberculin). The temperature showed sometimes slight elevations. The blood examination showed, (1) a leukopenia varying from 4,200 to 8,500 leukocytes; (2) a large amount of hemoglobin, a high count of erythrocytes (Table 2).

The spleen became slightly enlarged during the two months of residence at the hospital. Splenectomy was performed July 5, 1916.

TABLE 1.—BLOOD EXAMINATIONS BEFORE AND AFTER SPLENECTOMY
IN CASE 6

Date	Hb., per Cent.	Red Blood Cells	White Blood Cells	Neu- tro- phils, per Cent.	Eo- sino- phils, per Cent.	Baso- phils, per Cent.	Lym- pho- cytes, per Cent.	Trans- fusi- on, per Cent.	Türk, per Cent.	Total Lympho- cytes
5/10/16	81	4,540,000	5,000	38.7	2.2	0.7	55.0	3.2		2,750
5/17/16	75	5,020,000	4,600	41.2	4.7	0.2	52.2	1.5		2,400
6/ 6/16	..			46.2	8.5		45.2	5.0		
6/17/16	..		6,200							
6/26/16	..		4,400							
6/30/16	..		5,050							
7/ 8/16	..		4,250							
7/ 7/16	80	4,645,000	3,550	45.3	1.6	0.6	49.0	4.0		1,740
Operation, July 18										
7/20/16	76	5,750,000	23,150	72.4			22.6	8.8	0.2	5,230
7/22/16	81	6,510,000	20,000	62.6	1.4	0.6	32.0	8.8		6,400
7/24/16	81	6,360,000	19,975	45.0	6.5		45.0	2.7	0.7	9,000
7/31/16	88	6,370,000	17,625	56.7			39.2	4.0		6,900
8/ 7/16	85	4,360,000	14,175	25.0	8.5		60.5	2.7	3.2	8,575
8/ 8/16	..	4,570,000								
8/14/16	84	6,260,000	17,225	29.7	3.7		63.5	2.5	0.5	10,990
10/ 7/16	86	4,600,000	19,650	22.8	6.0		66.4	3.4	0.4	13,060
10/26/16	86	4,815,000	21,000	33.0	14.0	1.25	51.7	3.7		10,860
Normal at age of 7-8 years.....	78	5,042,860	8,353	60.18	3.69		27.98	7.75		2,337

The mother said that the enlargement of liver and spleen was already noticed in the sixth child when 4 years old; in the seventh child when 2 years old. There is every reason to believe that the disease in question is congenital in origin.

The occurrence of the positive Wassermann reaction does not

seem to be constant in those cases. In the case of Patients 6 and 7 the reaction was, in the beginning, slightly positive. On later examination, carried out by another serologist, the test was slightly positive in the case of one girl, negative in that of the other child; on third examination, performed by the same serologist, the reaction proved negative in both instances.

TABLE 2.—BLOOD EXAMINATIONS BEFORE AND AFTER SPLENECTOMY
IN CASE 7

Date	Hb., per Cent.	Red Blood Cells	White Blood Cells	Neu- tro- phils, per Cent.	Eo- sino- phils, per Cent.	Baso- phils, per Cent.	Lym- pho- cytes, per Cent.	Trans- luc- ids, per Cent.	Türk, per Cent.	Total Lympho- cytes
5/19/16	79	4,140,000	4,250	58.2	4.6	0.3	34.6	1.6		1,470
5/27/16	82	5,460,000	4,600	45.5	7.0		46.2	1.2		2,125
6/14/16	85	5,200,000	6,950	45.7	3.2		47.7	3.2		3,315
6/15/16	..		8,500							
6/16/16	..		5,900							
6/19/16	..		6,650							
6/23/16	..		6,350							
6/27/16	..		7,250							
7/ 1/16	53	5,750,000	4,375	54.0	3.0	0.5	36.0	6.5		1,575
7/ 5/16	80	5,000,000	4,200	48.5	3.5		46.5	1.5		1,953
Operation, July 5										
7/ 7/16	86	5,600,000	18,250	73.8	0.2	0.2	11.6	8.4	0.4	2,117
7/ 9/16	85	5,680,000	18,750	63.0	7.0		22.7	7.2	0.2	4,158
7/12/16	..	6,200,000	13,500	54.0	8.2	1.0	33.5	4.8	0.4	4,522
7/17/16	84	5,200,000	14,300	55.8	9.6	1.2	30.2	7.0		4,318
7/20/16	81	4,900,000	9,200	50.8	3.6	1.2	40.8	5.6	0.2	3,753
7/26/16	..		12,325	41.5	4.4	0.2	46.3	6.6	0.9	5,716
8/16/16	92	5,720,000	13,600	38.5	12.3		46.0	2.2		6,256
10/ 5/16	88	4,915,000	12,450	44.0	2.0	1.0	50.0	4.0		6,225
10/28/16	84	4,625,000	17,950	38.25	8.5	0.7	47.2	6.0		8,472
Normal at age of 5-6 years.....	77	5,189,000	9,813	55.39	6.22		31.04	7.85		3,042

While we collected the foregoing data about the children, we also examined the parents and three of the living grandparents.

The father, 45 years of age, was a dark, thin, strong man, always feeling well. He had never heard of any illness in his family; no enlargement of spleen or liver demonstrable on percussion or palpation; urine normal; no bile pigment present; urobilin test showed nothing abnormal; blood examination was performed three times. The normal figures are given first, Table 3.

The first examination shows a slight leukopenia; the second and third show figures which are practically normal, although somewhat low; a relative lymphocytosis was always present. We want to emphasize this point, although we do not venture to state that the origin of the disease in the children can be traced back to the father. We get the distinct impression, however, that in such cases an examination of the family ought to be carried out as carefully as possible.

The mother, 44 years of age, was a dark, healthy, well built woman; spleen and liver not enlarged; the left kidney, floating, was easily palpable. The blood count showed the following figures: hemoglobin 92 per cent. (Sahli); erythrocytes 5,350,000; white cells 6,070; differential count: polynuclear neutrophils 55.9 per cent.; eosinophils 4 per cent.; lymphocytes 35.3 per cent.; transitional cells 5.3 per cent.; Wassermann test negative.

Paternal grandmother, 71 years of age, of dark complexion (both Children 6 and 7 bear a marked resemblance to her). She had been married twice; had twelve children; five died in infancy; once she had twins; once a premature

TABLE 3.—RESULTS OF BLOOD EXAMINATION OF FATHER OF CHILDREN

	Hb., per Cent.	Red Cells	White Cells	Neutro- phils, per Cent.	Eosino- phils, per Cent.	Baso- phils, per Cent.	Lympho- cytes, per Cent.	Transi- tionals, per Cent.
Normal	..	5,187,000	6,800	60.7	2.4	0.5	20.25	3.5
5/25/15	88	5,340,000	5,200	82.2	2.4	1.4	61.8	4.8
6/ 8/16	..		6,875	45.7	3.8	0.2	46.2	0.2
11/ 1/16	..		6,425	42.0	1.6	2.0	50.3	4.0

birth. The other children were well; their offspring were also in good health. She never heard of any disease in her family like that of her grandchildren. Neither liver nor spleen was palpable; Wassermann test negative. Blood examination: hemoglobin (Sahli) 81 per cent.; red cells 4,918,000; white cells 9,100; differential count: polynuclear neutrophils 54.3 per cent., eosinophils 1.6 per cent.; lymphocytes 40.6 per cent.; transitional cells 3.1 per cent.

Maternal grandfather, 74 years of age, never had been ill; blonde complexion; no abnormal findings on examination. Blood count: hemoglobin (Sahli) 90 per cent.; red cells 4,950,000; white cells 8,250; polynuclear neutrophils 48.5 per cent.; eosinophils 1 per cent.; basophils 2 per cent.; lymphocytes 43.6 per cent.; transitional cells 5 per cent.; Wassermann test negative.

Maternal grandmother, 73 years of age, had always been well; had nine children, of whom three died (whooping cough, pneumonia, debility). She had never heard of any special disease in her family. Liver and spleen not enlarged. Blood examination: hemoglobin (Sahli) 87 per cent.; red cells 4,135,000; white cells 5,820; differential count: polynuclear neutrophils 49.3 per cent.; eosinophils 0.6 per cent.; basophils 0.6 per cent.; lymphocytes 45 per cent.; transitionals 5 per cent.

Based on the foregoing data no other clinical diagnosis but splenomegaly of Gaucher seemed to us possible. We will not consider in detail the differential diagnosis.

What is the prognosis in cases suffering from this disease? A

number of cases seem to take a very slow course. Observations are known where the patients died at the age between 30 and 50 from intercurrent diseases, but we also know of cases in which the disease was the cause of death on account of hemorrhages. In the foregoing cases the disease was decidedly progressive. One child, and probably two children, had fallen a victim to the disease. The oldest of the two girls, taken into the hospital, had begun to show signs of cachexia. We considered ourselves justified in proposing surgical interference. Both cases were successfully operated on by Dr. J. Ph. Backer, consulting surgeon of the hospital.

The operation on the younger child (Case 7) was performed first. No adhesions were found, no noticeable hemorrhage took place. After splenectomy the liver was entirely accessible to palpation, its surface smooth; the left hepatic lobe was firmer than the right.

The spleen weighed 170 gm. (about four times the normal weight). Its dimensions were, length, 12.5 cm.; breadth, 6.5 cm.; thickness, 3.5 cm. The shape



Figure 1

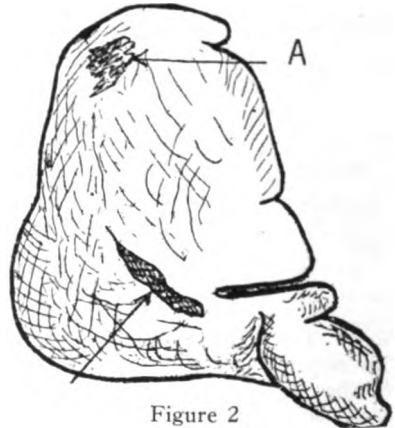


Figure 2

Figs. 1 and 2.—Spleen in Case 7, showing the outline and place of adhesions to the stomach at A.

was normal, but a deep incisure was present running from the center behind to the right upper part. The consistency was firm, the color grayish-red. The surface was slightly nodular, the nodules somewhat more brownish red than the deeper spots between. On further examination of the interior the color was found grayish red, the capsule was not thickened, the connective tissue somewhat more noticeable than usual. The follicles were remarkably distinct and large, more or less transparent. The organ was not very hyperemic; its tissues were firm; the pulp was not easily removed. An accessory spleen the size of a pea and two lymph nodes were removed. The microscopic examination gave in both cases the same findings, which we will discuss later. No special incidents were to be noted after the operation.

Blood examination showed an increase of leukocytes to 18,000. Temporarily, a slight albuminuria occurred; there was no increase of urobilin. The liver decreased somewhat in size after the operation; since then its size has remained stationary (three months *post operationem*).

The operation on the second child was more difficult. The spleen proved to be adherent to the stomach and the head of the pancreas; adhesions were broken

up carefully; no hemorrhage (Figs. 1 and 2). The spleen weighed 470 gm. (eight times the normal weight). The shape was somewhat disfigured. Large incisures were seen; at the right lower margin a very marked incisure was noticed, almost separating one lobe from the remaining body. Its dimensions were: length, 14 cm.; breadth, 13 cm.; thickness, 5.5 cm. Its surface showed a number of small nodules, varying in size. The color of the surface was purple-gray; small yellow patches could be distinguished. The organ was hyperemic; felt firm; at the hilus blue-red lymph nodes were present; during the operation similar nodes were seen on the pancreas. On further examination the capsule was found not thickened; there was much connective tissue; follicles clearly visible, more or less transparent; pulp not easily removable; hemorrhages at different places. Fourteen lymph nodes were removed from the hilus.

This child also stood the operation satisfactorily. There occurred a leukocytosis of 23,000 white cells. After the operation a marked urobilinuria occurred intermittently. The liver increased, first slightly, and returned later to its size preceding the operation (three months *post operationem*). In the summer of 1917 we found the children in good health.

Microscopic Examination of the Spleen, Accessory Spleen and Lymph Nodes.—Immediately after the operation samples were taken from the pulp and stained after the panoptic method of Pappenheim (May Grünwald and Giemsa). Scrapings were examined in normal saline solution. Some sections were frozen and cut. Some small pieces were put in alcohol *au tiers* of Ranvier and studied a few hours later. No large cells, which have been described in such cases, were found. From ten different places of each spleen, sections were made and hardened in absolute alcohol, formaldehyd and solutions of Orth, Flemming and Müller. We stained with hematoxylineosin; Leishmann's and Pappenheim's solution, after van Gieson, Mallory, Bielschowsky and with sudan III and hematoxylin. Large cells were not seen. Accessory spleen and lymph nodes were examined likewise.

One lymph node showed a small tuberculous lesion (positive von Pirquet's test). Neither spleen contained treponema (Levaditi's method). On examining macroscopically one of the slides, stained with hematoxylin eosin, the follicles were immediately noticeable because of their abnormal size and germinative center. The size of most of them varied between 0.5 and 1 mm. Microscopically some follicles, especially the smaller kind, showed absence of the large germinative center. Some germinative centers were surrounded by a zone of small lymphocytes, closely arranged together, in their turn surrounded by a zone of more scattered lymphocytes. The marked difference between center and environment was caused by concentric fibers, along which the lymphocytes were located. The cells in the center looked like large lymphocytes, with somewhat more protoplasm and nuclei somewhat less stained than those of the smaller lymphocytes, but the center was more dense and many cells were larger than usual. The cells in the germinative center showed, ordinarily, two or three distinct nucleoli, although some of them had only one nucleus and a pale protoplasm. These cells remind us of those which were first described by Bizzozero and later more carefully studied by Tatiana Waschkewitsch.¹ They are especially found in cases of diphtheria and pyogenetic processes. Probably a few of those cells occur normally in each follicle. Itami² also studied those cells. They apparently originated partly from lymphoblasts or lymphocytes, partly from endothelial cells. We found some of them in the follicular periphery and some in the splenic pulp, which seems to occur also under normal circumstances. Like Waschkewitsch we found the nucleoli of those cells red in slides stained after van Gieson's method. Some phagocytes were found in the germinative centers and a varying number of karyokinetic figures in the lymphocytes and "tingible Körper" of Flemming in and outside of the cells.

1. Waschkewitsch: Virchows Arch. f. path. Anat., 1900, 159.

2. Itami: Virchows Arch. f. path. Anat., 1909, 197.

This number varied, but was larger than usual, both in the spleens, accessory spleen and lymph nodes. Some follicles were noticeable for a thickened vascular wall. In the follicular periphery some polynuclear eosinophil cells were found. The slides stained after Mallory's and Bielschowsky's methods showed no changes of the intrafollicular structure; a few fine fibers between the cells were seen.

The picture of the splenic and lymphnodular follicles of our cases shows a marked resemblance to that which Flemming,³ in his classic study, gives of the secondary follicles in mesenterial bovine lymph



Fig. 3.—Photomicrograph of a section of the spleen in Case 7.

glands. Möbius⁴ saw the same thing in the spleen of full grown rabbits. He mentions having seen also in the pulp a few karyokinetic figures, something which we also noticed. In our slides, made from fifty cases of spleens studied in children, we never saw a greater activity of the germinative centers.

3. Flemming: *Arch. f. mikr. Anat.*, 1885, **24**.

4. Möbius: *Arch. f. mikr. Anat.*, 1885, **24**.

In the case of the oldest child, already referred to, the follicles could hardly be called normal. Besides some cells of Bizzozero-Waschkewitsch's type, we saw in the follicular periphery and in the pulp a few cells resembling large lymphocytes. The connective tissue was increased, both as to the trabeculae and the reticulum. Strips of spindle cells in bundles, containing connective tissue, ran through the pulp. The pulp showed some hemorrhages. The venous sinus was wide. Granulocytes in the pulp were easily seen (Leishmann's stain), the majority of which represent, in the case of the older child, polynuclear eosinophils. The splenic pulp in the younger child showed more myelocytes,

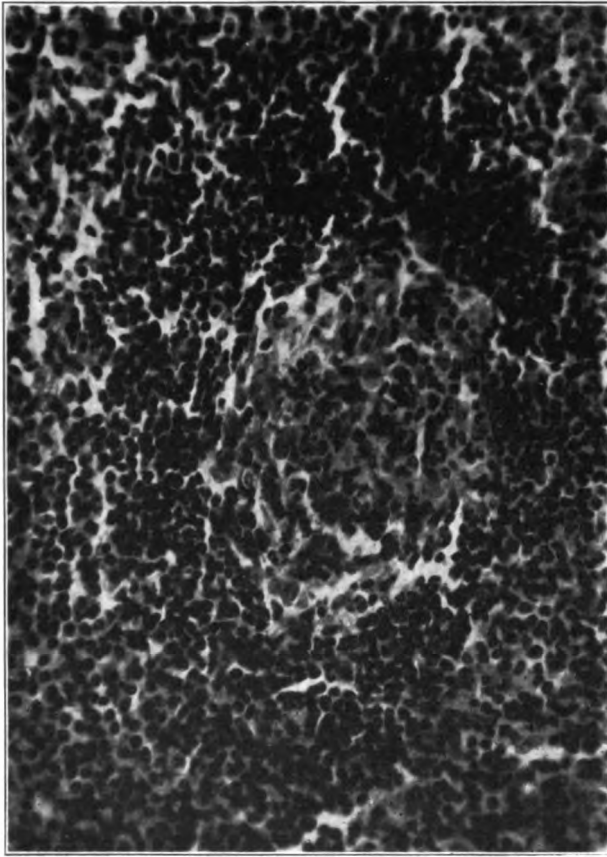


Fig. 4.—Higher magnification of section of spleen shown in Figure 3.

mostly eosinophils, a few neutrophils; some pigment was found in the trabeculae, lying free in the pulp, not in the endothelial capillary cells. Figure 3 represents a photomicrograph of one of our slides (slightly magnified), while Figure 4 shows the same picture greatly magnified.

The accessory spleen gives the same picture as the spleen. Many karyokinetic figures were noted in the follicles. Both lymph nodes showed an unaltered structure. They were hyperemic; nowhere were there large cells, but the follicles resembled the heretofore described splenic follicles. The fourteen lymph nodes of the older child showed varying pictures. They were

all hyperemic; the number of follicles with large, well defined germinative centers was variable; also the degree of karyokinesis. Some glands had follicles with a light center; others had practically none. Nowhere were follicles seen such as those noticed in the spleen, which showed a germinative center surrounded by a darker and a lighter zone.

Finally, we attempted to demonstrate lipoids. In both spleens a number of sudanophil cells were found in and outside of the follicles. As Kusunoki⁵ found those cells regularly in his examination of 132 spleens, we cannot see anything abnormal in their presence. According to Kusunoki, lipid cells are found in the follicles of the spleen of children, whereas in adults they are seen in the pulp. Possibly those cells represent the cells demonstrated by Bizzozero and Waschkevitch. The foregoing microscopic pictures have no resemblance to the pathologic findings in Gaucher's disease. There the normal splenic pulp has disappeared entirely, or almost entirely, and has been substituted by alveola-like sinuses, separated by more or less thick fibrous structure, filled with the well known large endothelium-like cells. The follicles in those instances are underdeveloped.

Originally we thought our cases could be considered as a juvenile type of Gaucher's disease and were supported in our opinion by a case described by Reuben⁷ and Mandlebaum⁸ concerning a boy 4½ years of age. In this case very large follicles, with noticeably active germinative centers, beside the familiar large cells, were found in the spleen and lymphnodes. Mandlebaum⁸ considers that the large cells originate from atypical lymphocytes of the germinative centers. We must acknowledge that no pathologic tissue was found in the examined organs (spleens, accessory spleen and lymph glands). Hypertrophy was the only finding.

Some years ago Dr. R. de Josselin de Jong,⁹ pathologist of the city hospital of Rotterdam, described a case of Gaucher's disease. After examining our specimens he believes that our cases have no connection with the disease mentioned. We have apparently to deal with a congenital *vitium primae formationis*, on account of which the spleen has developed into a state of "giant growth." Whatever the truth may be, we are dealing in the foregoing cases with a familiar progressive disease of the spleen which produces, sooner or later, an increasing cachexia, and in the course of which a hemorrhagic diathesis occurs *ante mortem*. Our clinical material may show us in the future similar cases, cases which we have not found mentioned before in medical literature.

5. Kusunoki: Ziegler's Beiträge Bnd. 59, 1914.

6. Nederl. Tijdschr. v. geneesk., 1917, No. 12.

7. Reuben, M. S.: AM. JOUR. DIS. CHILD., 1912, **3**, 28, and 1914, **8**, 336.

8. Mandlebaum: Jour. Exper. Med., January, 1914; *Ibid.*, 1912, **16**, 6.

9. De Jong: Nederl Tijdschr. v. geneesk., 1910, Nos. 8 and 9; Beitr. z. Path. Anat. u. z. allg. Path. (Ziegler's), 1910.

THE HYDROCEPHALUS OF POLIOMYELITIS *

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So prominent is this symptom of hydrocephalus in the pathologic and clinical picture of poliomyelitis, and so important is it from the viewpoint of treatment, that it seemed advisable to speak of it at length, and at the same time to show the value of Macewen's sign in its recognition.

In order to adequately discuss the hydrocephalus of poliomyelitis, it is necessary first to understand the pathologic basis for the symptom. Recent researches have shown that the earliest microscopic change that is found in the cord and brain is hyperemia and the collection of small mononuclear cells in the perivascular lymph space of the blood vessels of the leptomeninges. A sheath of cells is thus often formed completely encircling the vessel for a considerable length. This sheath may be so dense that the lumen is encroached on and the circulation is partly obstructed. Draper, Peabody and Dochez¹ think there may be some effect either toxic or mechanical which acts on the intimal lining of the blood vessel walls, for hemorrhages, minute or extensive, are frequent findings, and one of the pronounced features of most cases is the extensive edema. Wickman,² in his classical monograph, points out that edema may be so great as to appear to the naked eye like a general softening of the cord, and also that the brain may be so edematous that the dura is rendered tense and the convolution flat. He says that microscopic examination shows the walls of the veins to be more infiltrated than those of the arteries. Romer³ also notes the intense edema often encountered and the greater tendency for the infiltration to involve the veins. In the twenty odd cases of poliomyelitis necropsied at the hospital during the epidemic of 1916 by Regan and Rosenthal, there has been likewise a generalized edema, more

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1. Draper, G., Peabody, F. W., and Dochez, A. R.: Monograph 4, Rockefeller Institute for Medical Research, New York, 1912, p. 20.

2. Wickman, Ivan: Nervous and Mental Diseases, Monograph 16, New York, 1913, p. 14.

3. Romer, P. H.: Epidemic Infantile Paralysis, New York, 1913, p. 104.

markedly so in some cases than in others. Thus macroscopically the cord would usually be bulging between the strands of pia mater which covered it, and on cross section had a moist translucent appearance, and would often evert over the edge of the membrane as a collar. The consistency was softer than normal. Not infrequently the brain was so closely crowded against the calvarium that the convolutions of the superior aspect were decidedly flattened in places. In such instances the ventricles have been enlarged and evidently during life were distended with fluid. As in the case of the cord, the cut surface of the brain had a moist, translucent appearance, and was definitely of a softer consistency than normal, so that it was often a very difficult task to remove it intact from its bony envelope.

That edema should arise from diverse causes is not surprising when consideration is given to the particular type of pathologic alteration that occurs in this disease. Several factors especially predispose to the supervention of such a condition. Thus, the return flow of lymph from the tissues of the cord and brain, which probably normally passes in part along the perivascular sheaths of the blood vessels, is partially, and, in some cases, almost completely interfered with by the infiltration of round cells. Moreover, this infiltration being more intense in the veins than in the arteries, and the lumen of the former vessels being more easily obstructed by changes within their walls, owing to a less rigid structure, the venous return flow is more hindered than the arterial inflow, with a resultant tendency toward venous stasis and hence toward edema. Then, again, there may be a greater permeability to the intima of the vessels, which allows of serous exudation. It is, moreover, by no means improbable that the generalized inflammatory reaction of the nervous system may involve the pacchionian bodies to a sufficient extent as to interfere materially with the excretory function which they are normally supposed to exercise.

In addition to the edema of the tissues, there is present in a high proportion of the patients an actual increase in the quantity of spinal fluid in the subarachnoid spaces and in the ventricles of the brain. This is obvious before death, by the large quantities of fluid commonly removed by lumbar puncture, and postmortem, by the increased amount present in the subarachnoid spaces and ventricles, especially when the necropsy is performed a very short interval after death. A similar observation postmortem has been made by Wickman and by Romer. The choroid plexuses of the ventricles, especially the lateral, which are, according to our present knowledge, the secretory organs for the production of spinal fluid, are composed of anastomosing arteries and veins, and no doubt are intimately connected with hypersecretion. Poliomyelitis is accompanied, as we know, by an increased hyperemia of the brain, and this hyperemia involves naturally the

blood vessels of the choroid plexus. In addition to this, Draper⁴ claims that the perivascular infiltrations of the blood vessels may also involve those of the plexus. This being so, and the veins of the choroid probably being more concerned than the arteries, there is a distinct tendency toward interference with the venous return flow despite the active arterial supply. As a result of these various factors, hypersecretion results, producing an increased intracranial pressure, which reflexly causes a rise in the arterial and venous pressure throughout the cerebral circulation. Normally the excretion of the cerebrospinal fluid through the sinuses seems to depend on the fact that the intracranial pressure is slightly higher than the pressure in the veins. With the pressure in the veins raised equally with the intracranial pressure, excretion through the pacchionian bodies into the sinues is greatly retarded if not almost arrested, and further accumulation of cerebrospinal fluid occurs in the ventricles and subarachnoid spaces. This, in conjunction with the generalized edema of the tissues, presents a typical picture of hydrocephalus and gives rise to the clinical symptoms which we shall now describe, after classifying them as follows:

1. The hydrocephalus of the onset, including the preparalytic and early part of the paralytic stages.

2. The hydrocephalus persisting after the first week of the disease and comprising three types: (a) a mild form commonly encountered in which there is only a slight increase in fluid and in which symptoms are practically absent; (b) a more severe form accompanied by symptoms of pressure; (c) a very severe type, more or less insidious in onset, indefinite in physical signs, and associated with evidences of progressive emaciation.

1. *The Hydrocephalus of the Onset.*—As has been described under the pathologic picture of the disease, the onset of the meningeal phase of poliomyelitis is accompanied by a marked increase in the spinal fluid content of the subarachnoid space. Coincident with this, symptoms of acute hydrocephalus appear. The child becomes drowsy or stuporous, the pupils dilated, and react rather sluggishly to light; irritability is often marked; the respirations and pulse become rapid and sometimes irregular; vasomotor flushings of various parts of the body appear. Ataxia, headache, rigidity of the neck and profuse sweating may also occur and be due in part to the same cause. All these symptoms are strikingly alleviated by lumbar puncture, and large amounts of fluid, 40 to 80 c.c., may be obtained under considerable pressure. Even after paralysis has supervened these symptoms often still persist unless relieved by puncture. It is, moreover, noteworthy that paralytic phenomena of the early stages may often be, in part, due to the edema

4. Draper, G.: *Acute Poliomyelitis*, Philadelphia, 1917, p. 35.

and the hydrocephalus, for not infrequently there will be definite improvement following relief of pressure. It is in such instances that Macewen's sign is of the utmost value, for by its use the suspected group of symptoms can be definitely interpreted and suitable treatment instituted.⁵ No doubt it is to be found present to some degree in practically all cases of poliomyelitis in the preparalytic stage.

2. *The Hydrocephalus Persisting After the First Week of the Disease.*—(a) The condition may be so mild that practically no symptoms are noticeable, yet often a slight Macewen sign will be present and lumbar puncture will yield an increased quantity of spinal fluid under slight pressure. This is the usual type.

(b) In other cases there may be distinct evidences of pressure, as shown by persistence of the dilated pupils, the headache, the drowsiness or stupor, rigidity of the neck and the irritability when disturbed. The headache, the ataxia, the rapid respirations, the pulse, and the elevated temperature may all remain for an unusually long period, and the cause be determined by the presence of a positive Macewen sign or of a bulging fontanel. One or two lumbar punctures, with the removal of sufficient fluid to bring the pressure to normal—about 20 drops a minute—will often be sufficient to dissipate the symptoms and not infrequently materially improve the prognosis with regard to paralysis.

We have occasionally encountered cases running a persistently high temperature, and a moderately increased pulse and respiration, in the second or early part of the third week of the disease, with no physical findings to account for the febrile phenomena, in which the performance of a lumbar puncture would often be followed by the subsidence of the symptoms (Cases 3 and 4). Sophian,⁶ in his clinical study of epidemic meningitis, noted cases of a somewhat similar character and attributed them also to hydrocephalus.

Patients with paralysis of the intercostal muscles alone or with slight involvement of the diaphragm not infrequently present periods in which the breathing gradually becomes more dyspneic and labored, the diaphragmatic action more jerky and irregular, the pulse rapid, the pupils rather dilated, and a nervous apprehension and irritability is manifest. At the same time perspiration often is notably profuse and Macewen's sign prominent. The removal of a sufficient quantity of spinal fluid will usually be followed by the disappearance of the alarming symptoms.

5. It seems extremely probable that an examination of the eyegrounds would also be of considerable value in establishing the diagnosis of hydrocephalus, especially if the condition had been existent for several days.

6. Sophian, A.: *Epidemic Cerebrospinal Meningitis*, St. Louis, 1913, p. 138.

(c) A persistent hydrocephalus of this type is the most serious and the most hopeless of the different forms, but luckily it is not common. We have only encountered it in a small number of our cases. It usually supervenes at times in patients with extensive paralysis, involving all four extremities and the intercostal muscles. These children were usually desperately ill during the first week or two of the disease, and although passing through the danger period, showed no signs of improvement either in their general condition or in their paralysis. On the contrary, a decided loss of weight and rapid shrinking of the subcutaneous tissues was noticeable. The loss of tissue rapidly assumed alarming proportions, despite the ingestion of large quantities of food (for the appetite is sometimes ravenous, owing no doubt to central involvement of the vagus nerve). Eventually, extreme emaciation appears, and trophic changes occur in the skin, especially over bony prominences, such as the buttock or the back of the head, heels, etc., with the production of deep ulcers which may extend to the bone and show no tendency to heal. The mentality of the child gradually becomes dull and he ceases to take any interest in his surroundings, and finally dies in a state of acute inanition. Lumbar puncture is entirely useless in such cases, as the edematous condition of the brain seems to have assumed a subacute or chronic course with no tendency to subside.

Heiman and Feldstein,⁷ and later, Sophian,⁸ in their excellent studies of epidemic meningitis, describe very similar cases, and, indeed, so close is the resemblance of most of the hydrocephalic symptoms in the two diseases that we have modified somewhat our classification after that which Koplik⁹ used in his scientific clinical consideration of the hydrocephalus of meningococcus meningitis.

REPORT OF CASES

CASE 1.—*Illustrating chronic hydrocephalus of poliomyelitis.*

No. 2195, G. D., aged 5 years; ill three days when admitted to the hospital, August 4; discharged Oct. 3, 1916.

The condition on admittance was poor. The child was fairly well developed and nourished, but rather oversized for his age. He laid in a stuporous condition, out of which, however, he could be somewhat aroused. Macewen's sign was a markedly positive one; the neck was rigid anteroposteriorly, less so laterally. The pupils were dilated, equal, and reacted to light. Breathing was shallow, abdominal, with slight costal movement of the lower ribs, evidently due to the diaphragm, the intercostal muscles being completely paralyzed. There was complete flaccid paralysis of both upper and lower limbs, with absence of reflexes. The heart sounds were of fair quality, but the pulse was rapid and of very poor volume. The abdominal organs showed no apparent alteration.

7. Heiman, H., and Feldstein, S.: *Meningococcus Meningitis*, New York, 1913, p. 204.

8. Sophian, A.: *Epidemic Cerebrospinal Meningitis*, St. Louis, 1913, p. 81.

9. Koplik, H.: Quoted by Heiman and Feldstein (Footnote 7), p. 197.

Lumbar punctures were performed on August 5, 11, 16 and 19, with the withdrawal of, respectively, 20, 32, 22 and 20 c.c. of clear fluid in the order named. The spinal fluid of August 11 showed no increase in cells; a few mononuclears were present, however; albumin, ++; globulin, ++; Fehling's test, +++; no organisms on smear or culture. Following the first puncture there was a slight improvement in the stupor, the child became apathetic and developed a ravenous appetite, crying more or less continually in a very feeble and indistinct voice for food. Despite the consumption of large quantities of nourishment the fulness of the subcutaneous tissues soon disappeared, the overlying skin becoming wrinkled, and over the bony prominences showed trophic changes. Thus, in the region of the elbows, knees, heels and buttocks there appeared large areas of discolored, unhealthy though not ulcerated skin. An examination of the eyegrounds by our ophthalmologist, Dr. Berry, August 16, showed a marked retinal congestion. August 18, the child developed a severe aphthous stomatitis, with the formation of creamy white plaques, almost 3 cm. in diameter, on the edges of the tongue, the insides of the lips and cheeks and along the gums. Mastication was rendered difficult for a few days, but the condition soon passed off. The child still remained in a condition of apathy, lying for hours in the same position, his eyes wide open, with a vacant, or, at times, anxious expression on his face, which had now assumed the shrunken appearance of an aged person. The pupils were widely dilated but reacted to light. The abdomen was sunken,

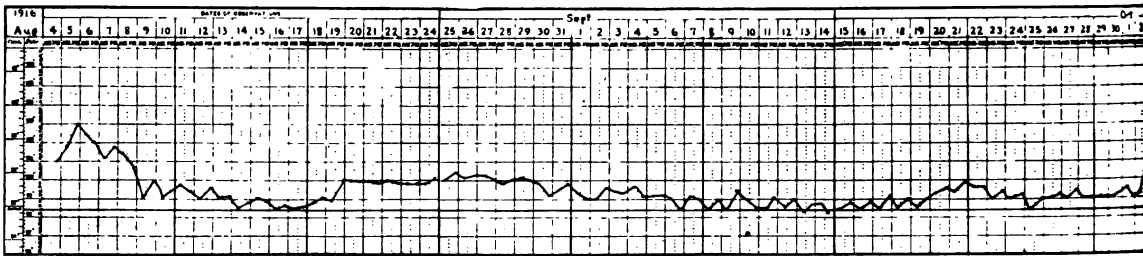


Fig. 1.—Temperature curve, G. D., Case 1 (No. 2195).

giving it a scaphoid appearance; the upper chest was constricted and narrowed, consisting only of the bony framework and the overlying skin. The lower chest was flaring, due to the unopposed action of the diaphragm and the thoracic and abdominal pressure during inspiration. The legs and arms became extremely emaciated; indeed, to such an extent that one hesitated to move him for fear of spontaneous fractures or dislocations. For hours at a time the child would cry, or rather whine, in a feeble voice. Not infrequently his actions and the few words he spoke that were understood indicated a clouded mentality and that he was suffering from hallucinations. The temperature and pulse remained slightly elevated and were subject to irregular daily variations (Chart 1). There was complete incontinence of urine and feces. The patient was discharged October 3, and the subsequent history was not obtained.

Remarks: This case showed the rapid and extreme wasting, which is also commonly seen in the chronic hydrocephalus of meningococcus meningitis, and this despite the ravenous appetite of the patient. The altered mental condition is also especially worthy of notice.

CASE 2.—Also illustrating chronic hydrocephalus.

No. 1778, H. O., aged 4 years; taken ill two days before admission; admitted July 24, died Sept. 2, 1916. The condition on admission was very poor, pulse barely perceptible, extremities rather cold, some cyanosis of skin and mucous membranes. The child was in a condition of deep stupor; could not be aroused

and was entirely unconscious of her surroundings; Macewen's sign was markedly positive; pupils dilated but reacted sluggishly to light; neck was flaccid; respirations were shallow, slow, and costo-abdominal. Evidently the intercostals were completely paralyzed and the diaphragm was working poorly. The knee jerks and plantar reflexes were absent. There was no Kernig sign, nor was there any polyneuritis. Paralysis involved almost the entire body—both uppers and lowers, back, neck and intercostals—and was flaccid in type. In addition, the cranial nerves were concerned; thus, there was a right internal strabismus, evidently due to paralysis of the abducens, a partial paralysis of deglutition, due to involvement of the glossopharyngeal or vagus nerves, and probably a laryngeal paralysis due to affection of the laryngeal branches of the vagus. A direct laryngoscopic examination was impossible owing to a spastic condition of the jaw muscles—"trismus"—which also rendered feeding difficult at first, except by gavage and nutrient enema. The heart sounds were of good quality and distinct, but the pulse was of very poor volume. The abdominal organs were negative; the nutritional condition and development fair; the conjunctiva injected, and there was a slight mucopurulent discharge.

Spinal puncture was performed on admission and 50 c.c. of clear fluid under marked pressure were removed. Punctures were performed on the 26th, 27th, and 31st, and 45, 40 and 20 c.c. of fluid were removed, in the order named. The examination of the spinal fluid of July 26 showed albumin + + +, globulin + + +, Fehling's + + +; cells not specified; no organisms on smear

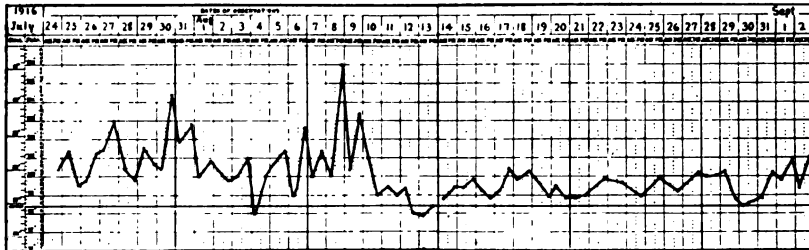


Fig. 2.—Temperature curve, H. O., Case 2 (No. 1778).

or culture. That of July 27 showed a slight increase in cells, 99 per cent. large mononuclears; albumin +, globulin +, Fehling's test + + +; no organisms on smear or culture. There was a slight improvement in the stupor after the second puncture, and this continued, but was only to a relatively unimportant degree, the patient still lying in an apathetic state, but showing some desire for food. The respiration was less dyspneic, deglutition was somewhat easier and the pulse improved following the punctures. A rapid emaciation set in, however, almost from the start, and it was out of all proportion to the loss entailed by the diminished ingestion of food. This symptom soon became so pronounced that the patient's body was composed only of the bony framework and skin; it might truly be said that the child was a living skeleton. The upper and lower limbs became flexed at the elbows and the ankles; pressure or trophic changes occurred in the skin, over the buttock and at the back of the head. In the latter position a large indolent ulcer, comprising the entire back of the head, was formed, with the bone devoid of periosteum as its base. There was complete incontinence of urine and feces. The patient laid in this condition day after day, until death occurred in the sixth week of the disease, with the symptoms of respiratory paralysis.

Remarks: In this case the partial paralysis of deglutition and the "trismus" rendering feeding difficult at first, would of course account for some wasting. But the emaciation appeared from the start, and was too extreme to be due to this cause alone. Moreover, there were other cases equally as difficult to

feed, who in the same length of time showed not nearly the same degree of inanition. There was also present a mental deterioration very similar to that noted in the previous case.

CASE 3.—*Illustrating persistently high temperature, with no physical signs to account for it except a condition of distinct hydrocephalus.*

M. W., No. 2559, aged 3 years; ill two days on admission, Aug. 12, 1916. Discharged Oct. 5, 1916. Physical examination on entrance showed a well developed and well nourished child, very irritable, and desiring to be left alone; crying frequently during the examination; evidently hyperesthesia was intense. The pupils were equal, rather dilated, and reacted to light. Macewen's sign was present and rather marked. The neck was not rigid but flaccid, and did not support the head. The patellar reflexes were absent; plantars were present but sluggish. There was a modified Kernig sign in both legs. The breathing was costo-abdominal in type, but somewhat shallow. Both legs were partially paralyzed, also the neck. The back was rigid, and there was a right internal strabismus present. The heart and lungs as well as the abdominal organs showed no detectable pathologic change. The temperature was 101 F. on admission and remained persistently at the same level, except for variations of one or two tenths of a degree, until August 17, and this despite the absence of obvious physical signs to account for it (Chart 3). Owing to the presence of symptoms pointing to hydrocephalus a lumbar puncture was per-

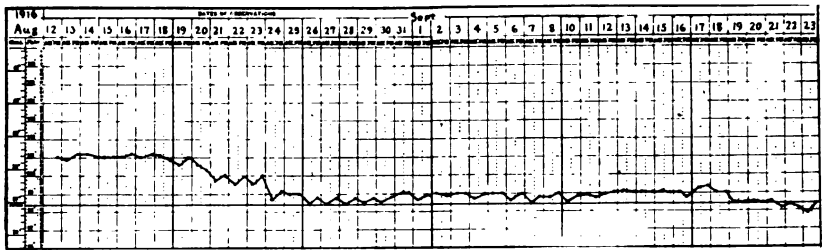


Fig. 3.—Temperature curve, M. W., Case 3 (No. 2559).

formed on this date with the withdrawal of 28 c.c. of clear fluid under pressure, followed by the injection of 10 c.c. of normal horse serum. As the temperature remained still at the same level on the following day, the procedure was repeated and 20 c.c. of slightly opalescent fluid was withdrawn. Following this withdrawal the temperature began to fall by lysis, reaching the normal August 26. Accompanying this there was a fall in pulse rate and a general improvement in the patient's condition, together with a subsidence of the meningeal symptoms—hyperesthesia, irritability, Macewen's sign, Kernig's sign—and the breathing became deeper. The paralysis improved soon to such an extent that the child could sit up in a chair. Having once attained the normal point, the temperature continued at 99 F. or thereabouts, throughout the rest of the time spent in the hospital.

Remarks: Hydrocephalus may cause a similar continuous elevation of temperature in other diseases. We have encountered it in complicated cases of measles, and in cases of epidemic meningitis, and it has also, in these instances, yielded to rachiocentesis.

CASE 4.—J. W., aged 4 years, No. 2560, was admitted August 12 and discharged Sept. 5, 1916; ill two days before entrance to the hospital. The patient was a sister of the patient, Case 3. The clinical symptoms and history were very similar with the exception that in this case the temperature remained persistently at 103 F. for three weeks. Two lumbar punctures were performed, with the removal of 25 c.c. and 30 c.c. of clear fluid on August 14 and 17,

respectively, and while the temperature subsided somewhat after the 17th and the meningeal symptoms improved, neither disappeared till two weeks later. The examination of the spinal fluid of August 14 showed fibrin present, slight increase in cells, 98 per cent. mononuclears, albumin, ++; globulin, ++; Fehling's test, +++; no organisms on smear or culture; while that of August 17 showed the presence of fibrin, slight increase in cells; 99 per cent. mononuclears; albumin, +; globulin, +; Fehling's test, +++; no organisms.

Remarks: It is probable that had the punctures been repeated persistently, convalescence would have been considerably hastened.

CASE 5.—Illustrating persistent hydrocephalus, with the symptoms of toxemia, and a prolonged elevation of temperature as well as of a marked polyneuritis but without extreme emaciation.

J. E., No. 3074, ill four days before entrance; admitted Sept. 3, 1916; discharged Oct. 24, 1916. On admission the child was fairly well developed and nourished, but was acutely and desperately ill. He was extremely irritable, crying on the least handling; evidently hyperesthesia was marked. At the same time if he was not disturbed he became drowsy and laid in a condition of light stupor. Macewen's sign was a markedly positive one. The pupils were dilated, even, and reacted to light. The neck muscles were flaccid. The breathing was costo-abdominal, but shallow, the costal movement comprising only the lower ribs and being evidently associated with the motion of the diaphragm, and not due to the intercostal muscles. The knee jerks were absent, the plantar reflexes were exaggerated and the abdominal muscles were normal on both sides. There was a modified Kernig reaction present which was accompanied by a great deal of pain. The child was unable to sit or stand. Paralysis involved the muscles of the neck which were flaccid, the intercostals, the right upper and both lowers, which were rigid, and the left upper extremity, which was flaccid.

There was marked hyperesthesia along the spine and polyneuritis along the posterior aspect of both legs and thighs. At times the child's respirations became rather jerky and irregular, and the skin somewhat cyanotic. The pulse was poor in volume and was rapid, but the heart sounds were of fair quality.

On September 4 the first lumbar puncture was performed, 20 c.c. of bloody fluid removed and 16 c.c. of serum injected. September 6 the child's condition was slightly improved, he was less drowsy, the respirations were somewhat fuller and less jerky, and the color and pulse better. September 8, 16 c.c. of convalescent serum were given by intramuscular injection. The blood count before the injection was: total leukocytes per c.mm., 6,900; polynuclear neutrophils, 61 per cent.; while on September 9 the count was 11,300 whites and 72 per cent. polynuclears; on September 10, 12,700 whites and 70 per cent. polynuclears. September 9 the second puncture yielded 28 c.c. of slightly opalescent fluid under pressure. The cells were moderately increased—97 per cent. mononuclears—the albumin, +; globulin, +; Fehling's test, ++; no organisms on smear or culture.

Between September 9 and 14 there was slight but continuous improvement, the child's general condition was better, he was less extremely irritable, cried less when handled, his extremities became less rigid and he began to use them slightly; the respirations became easier and deeper, the pulse improved. Macewen's sign became less marked but was still present to a moderate extent. The elevated temperature persisted, however, ranging around 101 F. There were no other physical findings in the lungs, heart or abdominal organs to account for it. Between September 14 and 18 the symptoms of irritability, more labored respiration, more marked Macewen's sign, again became conspicuous and another lumbar puncture was performed September 18, this time with the removal of 20 c.c. of clear fluid under pressure. The fluid showed a slight increase in cells, all mononuclears; albumin, +; globulin, +; Fehling's test, ++++. The symptoms were temporarily alleviated, but September 23 the procedure had to be repeated and 30 c.c. were obtained under marked

pressure. Examination showed moderate increase in cells, 98 per cent. mononuclears; albumin, +; globulin, +, Fehling's test, ++. September 25 the patellar reflexes had reappeared in the left leg, the rigidity had almost disappeared from the legs and arms, the breathing was deeper, the child's general condition was better, he was brighter and not so irritable, but it was noticeable that there had been a considerable loss of weight since admission. The elevated temperature still remained and continued so until discharge, with nothing other than the changes in the central nervous system to account for it. Macewen's sign was present throughout the period. The excitable, irritable, and "on edge" disposition, the polyneuritis of the lower limbs, remained to some extent, though improving slowly in conjunction with the paralysis.

Remarks: In some cases of poliomyelitis, like this last, for example, it would appear that the infection of the tissues of the central nervous system by the virus of the disease was of a persistent and deep seated character, not running its course in a few days or weeks, but extending over a long period of time and giving rise to the symptoms we have recorded. Whether the hydrocephalus is the predominant feature of these cases, or whether it is merely secondary to persistent infection or toxemia is difficult to decide. It is in such cases as these that one might well expect the causative agent of the disease to be given off in the nasopharyngeal secretions for several months after the acute period of the disease.

CASE 6.—Illustrating a very severe and almost fatal type of hydrocephalus, concomitant with the onset of the disease, but subsiding rapidly following rachiocentesis.

No. 3003, B. H., aged 8½ months; ill five days before admission, August 28; discharged Oct. 16, 1916. Examination on admission at 7 p. m., showed the child extremely cyanotic; the respirations were very shallow and somewhat stertorous and extremely irregular, being interrupted by periods of complete cessation of breathing for as long as two minutes. During these periods the cyanosis became extreme and artificial respiration was necessary. Macewen's sign was marked despite the presence of a bulging fontanel. The pupils were constricted and the eyelids tightly closed. The child was deeply stuporous. Apparently there was paralysis of both lower extremities present, but it was difficult to determine as the child was in a condition of extremis. Patellar, plantar, biceps, and abdominal reflexes were apparently absent. The respirations were abdominal in type, but very shallow.

At 9:30 p. m., a lumbar puncture was performed and 68 c.c. of clear, transparent fluid was removed under marked pressure, and 14 c.c. of horse serum were injected by the gravity method.

During the withdrawal of fluid and immediately following it for one and a half to two hours, the child had several attacks of severe and prolonged suspension of all respiratory movements, often for as long as one to three minutes at one time. At such periods there was generalized cyanosis and complete disappearance of radial pulsation. Artificial respiration was urgently needed during these periods to keep the patient alive. Between 11 p. m. and 3 a. m., August 29, the condition remained still one of "extremis," and oxygen was used almost continuously during each spell of apnea. It was given by Dr. Meltzer's apparatus for the administration of oxygen under pressure and quickly relieved the cyanosis. Hypodermic injection of atropin sulphate, ⅛₆₀₀ grain, and camphor, 2 grains, were also resorted to during this interval. After 3 a. m. the child improved. The spells of apnea disappeared, the cyanosis became less and the breathing deeper, while at the same time the radial pulse became of much better volume. The stupor lessened and the child began to take nourishment.

On the following day, August 29, a more complete physical examination was made. It gave the following findings:

The child was very well developed and nourished; rather drowsy; fontanels slightly tense but not bulging; slight rigidity (anteroposterior) of the neck;

pupils constricted, but reacted to light; left internal strabismus present; respirations were purely abdominal, but while shallow, were fairly regular, and there was no apnea. There was apparently no definite paralysis, except the strabismus. Patellar and plantar reflexes were normal. There was no Kernig's sign. The heart was rapid but the sounds were of good quality. The lungs showed some areas of bronchovesicular breathing, but no râles. The abdomen was distended. The liver was slightly enlarged, extending two fingers' breadth below the costal margin. The improvement in the child's condition, compared to the previous night, was simply astonishing. From the grave, almost moribund state on admission, he was transformed within twenty-four hours into a convalescent and merely by one spinal puncture. An examination of the spinal fluid showed a slight increase in cells; 98 per cent. mononuclears; albumin, +; globulin, ++; Fehling's test, ++.

August 31 the respirations increased to 40 and the temperature increased slightly. The child coughed frequently and there were some rather fine râles scattered in a few areas on both sides of the chest. This subsided in three days and convalescence was rapid and complete, the child being discharged with no residual paralysis except the slight strabismus.

Comment: This case shows an extreme form of hydrocephalus of the very acute stage, which would probably have terminated fatally but for the timely removal of fluid. The noteworthy thing is the rapid transition of the patient from a condition of extremis to convalescence in a few days.

SUMMARY

Researches pursued on the pathology of poliomyelitis have shown that edema is one of the prominent characteristics of the disease. Several factors especially predispose to such a condition: thus, the return flow of lymph from the issues of the cord and brain is interfered with by the cellular infiltration of the perivascular sheath of the blood vessel wall, while at the same time the veins being more infiltrated than the arteries and their lumen more easily obstructed, due to a less rigid structure, the venous return flow is more hindered than the arterial inflow, with a resultant tendency toward venous stasis and hence toward edema. These two factors in conjunction with the congestion accompanying the early stage of inflammation explain in part the edema. There may be concerned also some toxic effect acting locally on the blood vessel wall.

In addition to the edema of the nervous system, there is also an actual increase in the quantity of spinal fluid in the subarachnoid spaces and in the ventricles of the brain. This is obvious before death by the large quantities commonly obtained by lumbar puncture and postmortem by the increased amount found present. There is probably coincident with the congestion of the brain a hypersecretion of cerebrospinal fluid by the choroid plexuses and at the same time the excretion into the sinuses through the pacchionian bodies is temporarily unable to handle the increased amount produced.

Therefore it is not surprising that this condition of acute nonobstructive hydrocephalus should give rise to certain definite clinical symptoms. According to the type of symptoms and the time they

persist, we have found it advisable to divide the hydrocephalus of poliomyelitis into the following forms:

1. That of the onset (including the preparalytic and early paralytic stages).

2. That persistent after the first week of the disease and comprising three varieties: (a) a mild form commonly encountered in which there is only a slight increase in fluid and in which symptoms are practically absent; (b) a more severe form comprising various degrees, in which there are distinct signs of pressure; (c) a very severe type, more or less insidious in onset, indefinite in physical signs, and associated with evidences of progressive emaciation.

The symptoms of these various types are described under their suitable headings in the preceding text, and suitable case reports are included to amply explain these descriptions.¹⁰

Macewen's sign provides a definite means by which these symptoms of hydrocephalus may be easily recognized and suitable treatment by rachicentesis instituted, and therefore its employment in the routine physical examination of a patient with poliomyelitis is of the utmost importance.

10. Since an attempt has been made in this article to introduce a distinctly new clinical entity in reference to poliomyelitis, these descriptions and reports should be read in order to obtain the essential points.

EXPERIENCE WITH VACCINE IN THE PREVENTION OF WHOOPING COUGH *

FRANK VANDER BOGERT, M.D.
SCHENECTADY, N. Y.

Since the value of vaccine in the prevention and treatment of whooping cough is still not generally admitted, although the burden of proof seems unquestionably in its favor, the following experience with its use as a prophylactic measure seems worthy of report.

At the Children's Home in Schenectady, one of the forty-six inmates developed whooping cough on or about Nov. 27, 1917, but because of failure of diagnosis was allowed to mingle for nearly a week with other children, after which he was isolated in a separate building. It was later learned that during this time he was known to have whooped and vomited.

With the view of undertaking measures to prevent spread of the infection through the Home, an effort was made to confirm absolutely the diagnosis. An epidemic of the disease was well under way in the city at the time, and several of the whooping cough patients had been attending the school to which the children of the Home were sent daily, and at the time of writing, seven weeks after the development of the case, there were nearly 400 records of pertussis at the City Health Department, and the number of unreported cases, of course, cannot be ascertained.

As confirmatory evidence of the correctness of the diagnosis, the child was said to have whooped and was known to have vomited with the cough. A blood count showed a lymphocytosis of 61 per cent., and a smear from the pharynx gave many gram-negative bacilli, reported as suspicious of the Bordet-Gengou type.

Having apparently confirmed the diagnosis, the histories of the other inmates were examined for past record of the disease. Of these, thirty-one gave no record of having had whooping cough, although from the father of one we later learned of a past infection.

Dec. 3, 1917, the thirty-one were inoculated, each with 50 million plain pertussis vaccine (stock). All the inoculations were satisfactory, with the exception of that given to one new boy who was frightened, causing the needle to slip and the dose therefore to be doubtful. All the doses were carefully measured and were therefore practically accurate. No reactions were noted, but one child complaining of a sore arm.

Up to the present time (Jan. 24, 1918) not a single case has developed in the Home. The original case was given one dose of vaccine immediately after the diagnosis was made and ceased whooping at the end of one week. The vaccine was not repeated.

111 Union Street.

* Submitted for publication Feb. 12, 1918.

ABDOMINAL INJURY DUE TO BLUNT FORCE; DIFFICULT DIAGNOSIS *

HENRY P. DE FOREST, M.S., M.D.

NEW YORK

History.—Betty F., born April 17, 1913. With the exception of a mild attack of chickenpox two years prior to the accident to be described, the child had had no illness. Her physique was excellent and she was self-reliant and competent to an unusual degree.

Sept. 29, 1917, while riding astride her hobbyhorse on the lawn the horse reared over backward and the child fell on her back with her feet still astride the body of the horse. The back of the saddle, 2 inches wide and about 8 inches across, heavily padded with leather, fell directly across her body at the level of the navel. The right side suffered more from the blow than the left, and over the right lower ribs the child thereafter always placed her hand when asked where she was hurt or where she had pain. The accident was seen and the child was helped to her feet. She was badly frightened, but did not appear to be seriously hurt. After crying for a minute or two she went with her parents for a walk of about a half mile, without complaint.

She slept quietly during the night, but the next morning complained for the first time of a slight pain in her right side at the point already mentioned. Her parents thinking she had some intestinal trouble called the family physician, Dr. G. G. of Poughkeepsie. His examination disclosed nothing of special note and the child played about much as usual during the day, occasionally complaining of soreness in her side.

October 1 the physician was again called before leaving for a week's vacation, but found no new developments. So little importance was attached by the parents to the fall, that no mention was made to him of the accident at either visit.

That afternoon, however, the temperature, which on the previous day had been 99 F., and on that morning 100, suddenly rose to 103.5, and a competent surgeon was asked to see the child. He was told of the fall beneath the hobbyhorse and examined the hobbyhorse as well as the child. From the weight of the plaything (75 pounds) and the place of localized pain, a bruise of the intestines or other abdominal organs was considered possible. He asked that a medical man see the child, and the following morning she was seen by a pediatricist. On this day, October 2, I also was called in consultation.

Physical Examination.—Examination in the evening showed a marked point of tenderness definitely localized by the child at the lateral border of eleventh rib on the right side. The right half of the abdomen was tense, and the patient cried when she was touched. Shortly before my arrival her bowels had moved for the first time since the day after the accident. There was no blood in the stools, and their appearance was normal and so continued. It was decided that injury to the intestines was not probable and this factor was excluded.

Tentative Diagnosis.—The possibility of injury to the right kidney was then debated. The child had urinated regularly since the accident, the urine had been examined each time, and a specimen recently passed was examined by all three consultants and found to be free from blood and quite normal. The kidney therefore was also considered as probably uninjured.

* Submitted for publication Dec. 21, 1917.

* Read before the Clinical Society, New York Post-Graduate Medical School, Nov. 16, 1917.

The possibility of injury to the liver was next considered. There was no jaundice, the area of liver dulness was not enlarged; the free edge of the liver could not be felt below the costal border; there was no palpable tumor of the gallbladder, and while possible internal injury of this organ was also admitted, it was not believed probable.

Traumatic injury of the appendix was excluded, largely because of the location of the pain and the fact that pressure at McBurney's point gave no symptoms. An abnormal position of the appendix was considered, and this organ was not definitely excluded, though it seemed an improbable condition.

In view of the undoubted occurrence of a rather severe trauma due to blunt force, a definitely localized area of tenderness about an inch in diameter, and the evident pain and disturbance of the child, it was our opinion that some internal contusion undoubtedly existed. Whether this contusion was of sufficient importance to justify an exploratory operation was then discussed, and it was decided, in view of the fact that the temperature had fallen to 102 in the morning, and at the time of the consultation was only 102.2, that we should await developments and see the child again on the following morning. An icebag was applied to the right side, and the patient soon fell asleep and slept well during the night.

At the consultation early in the morning of October 3, the child's temperature was 100 F. Localized tenderness still persisted, but all of the other symptoms were improving. Her abdomen was less tense, and she was more comfortable. There was no evidence of any material loss of blood, and while we agreed that a hematoma existed, probably of the abdominal wall on the inside of the lower costal cartilages, an exploratory laparotomy did not seem advisable in view of the fact that conditions appeared to be improving.

Course.—During the following week the little patient was seen daily by Dr. C. October 7, he noticed and called the attention of the parents to the fact that the edge of the liver could now be felt about 1 inch below the free border of the ribs. This was the first time that abdominal palpation could be made without causing the child to cry from pain. On the 8th the family physician returned and found the patient up and dressed, playing much as usual and complaining of no pain. He saw her again on the 10th, 15th and 19th, and noted that the liver was apparently increasing in size. He believed that this was due to an excess of fat in the diet, which was modified accordingly. The temperature in the meantime, which had varied from 100 to 100.8 until October 9, fell to normal on the 9th and was not taken again for about two weeks.

During the last two weeks of the month the parents noticed that their child was becoming more and more languid, more and more pale, did not look or act well, and complained of difficulty in picking things up from the floor and of discomfort when sitting on the floor tying her shoes.

October 31, having been again called the physician found a large mass lying below the free border of the ribs on the right side. The child complained of sharp pain in her right side, coming on in spasms and causing her to cry out.

November 1, Dr. P. of New York was called as a consultant. He recognized the large mass in the right abdomen and expressed the opinion that it was the liver and that an abscess might be present, or that a new growth of some one of the abdominal organs, possibly the kidney, might be developing. The condition of hypertrophic cirrhosis of the liver was also suggested. The urine was found to be normal, and the blood showed marked anemia, but no leukocytosis.

November 3 I was again called in consultation with Dr. S., Dr. C., and Dr. G. The child was up and dressed, and came to the door to meet me. She was evidently very ill, showed a marked anemia, with extreme pallor, and about once an hour spasms of pain occurred. These symptoms also were very noticeable to Dr. S. who, like myself, had not seen the child since October 3.

Second Examination.—Examination showed that the abdomen was greatly distended and looked in outline not unlike a miniature pregnancy at full term.

The distention was greatest in the cephalic half of the abdomen, and an area of complete flatness existed from the level of the nipple on the right side to a line 4 inches below the level of the ribs. The caudal border of this area curved parallel to the free border of the ribs to a point midway between the navel and the ensiform cartilage and then curved downward on the left side in a similar manner. A border of dullness an inch in width followed this area of flatness. Through the abdominal wall a sharp curved border of a mass, presumably the free edge of the liver, could be easily palpated. The remainder of the abdomen was markedly tympanitic. This examination was made with ease, and at no time did the child complain of pain on pressure, though when asked to localize the spot that hurt her she always placed her finger at the original spot of soreness. The area of flatness extended around the right side to the vertebral column, and as low as the crest of the ilium (Fig. 1).

The child by preference lay on her back with her knees, particularly the right, partially drawn up and resting on a small pillow. She could be turned on one side or on the other without causing her to complain. No free fluid could be demonstrated in the abdominal cavity.

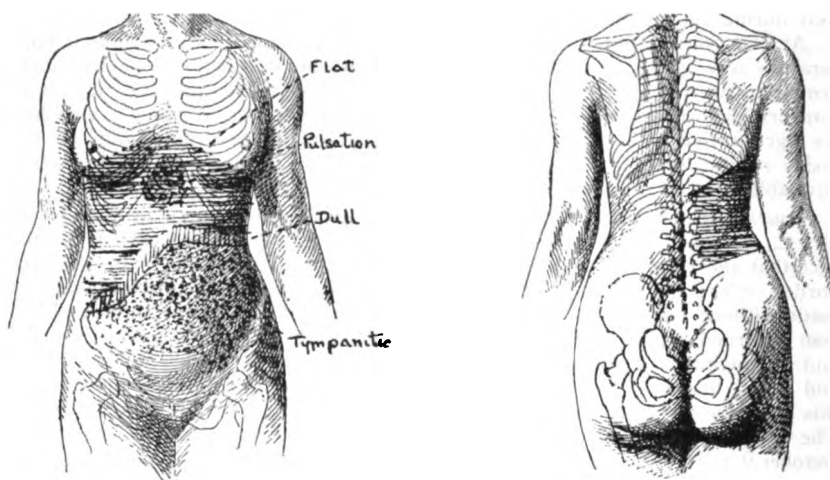


Fig. 1.—Physical signs found just before the operation.

The heart and lungs were normal, though the resonance of the lungs on percussion was noticeably increased, particularly on the right side. Breathing was rapid and shallow (24 to 30 per minute). Deep breathing at times caused the child to complain of pain at the original point of tenderness.

The temperature was subnormal, and taken by rectum ranged from 97 to 97.5.

Diagnosis.—At the consultation all agreed that injury to the stomach or intestines and appendix could, without doubt, be eliminated. The bowels by this time were regular, the stools were normal, and there had been none of the classical symptoms of appendicitis. An injury to the gallbladder was also excluded because of the absence of icterus and the fact that the urine at no time showed evidence of biliary absorption. No localized tumor existed at the site of the gallbladder, although immediately below the ensiform over an area 2 inches in diameter, undoubted fluctuation could be elicited on deep palpation. A possible intracapsular rupture of the liver, with subsequent infection from some low-grade bacterial organism was considered as being possible, although the clinical symptoms of chills, fever, and sweating were absent, and the blood examination showed no leukocytosis. While this condition, therefore, was admitted as a possibility, its probable existence was not believed. The sug-

gestion of there being a new growth of some abdominal organ, probably the kidney, was discussed, but this too, seemed improbable in view of the fact that the child had been an absolutely healthy child, and that the tumor mass, whatever it might be, undoubtedly took its origin from a distinct and localized trauma. Hypertrophic cirrhosis of the liver is occasionally observed in children at an early age, but there is always a history of previous malaise and of digestive disturbances. Free fluid in the abdominal cavity is practically always present. None of these symptoms could be demonstrated, and in any event the ultimate outcome is fatal. The abdominal mass so clearly felt on the right side had such a sharply defined edge, parallel with the costal line, that it was believed by all of us to be the free border of the liver pressed downward from above by some undetermined cause. The normal character of the urine both in quantity and quality during the entire month, and the complete absence of blood at any time in the urine seemed to exclude fracture of the kidney or rupture of the ureter, though both conditions were mentioned and discussed.

The extreme anemia of the child, the progressive increase of size of the upper abdomen, particularly on the right side, the point of the original injury, and the persistence of localized pain led to the belief that a hematoma was present, probably subphrenic in character, and firmly encapsulated, steadily extending across the abdominal surface of the diaphragm. This seemed the most probable diagnosis. The anemia, the steady increase of respiratory and cardiac oppression, the area of pulsation caudad of the ensiform cartilage, were regarded as indicating immediate surgical interference.

Arrangements were therefore made for an exploratory laparotomy on the following morning at the patient's home.

Operation (November 4).—Ether anesthesia was employed. No further information was elicited by examination under the anesthetic. An incision 6 inches long was made at the dextral edge of the right rectus muscle. As soon as the abdominal wall was incised, hemostasis secured and the tumor exposed, it was at once apparent that the mass was not the liver at all. A dense capsule existed with a sharp ventral border over which extended numerous enlarged veins. The liver was found to be entirely displaced to the left of the wound of operation, and the normal gallbladder was felt with difficulty 3 inches to the left of the ventrimeson. A part of the diaphragmatic surface of the liver was exposed, and showed no abnormalities. There were no ruptures of the liver, nor any evidence of an abscess cavity. The abdominal wound was walled off by sponges in the usual way and an aspirating needle passed into the fluctuating area thus exposed. About 2 ounces of clear straw-colored fluid were withdrawn, the last of which was tinged with blood. No odor of urine could be detected, and this fluid was believed to be supernatant blood serum. A 3-inch incision was then made and there at once escaped over a pint of blood, blood clots and a few soft, pale-gray masses much resembling in appearance the tissue of a small round-celled sarcoma. After this mass of partially organized blood clot and tissue substance had been removed, the operator's finger was able to reach around to the side of the vertebral column. The kidney appeared to be entirely disorganized and broken down. The tumor wall was evidently the capsule of the right kidney enormously distended. This sac was emptied as speedily and as thoroughly as possible, lightly packed with two long gauze sponges, a dressing applied and the patient put to bed. The entire operation took an hour. The relation of the encapsulated hematoma to the adjacent organs at the time of operation is shown in Figure 2.

Outcome.—The patient soon came out from the anesthetic and for an hour or two, although suffering from shock, seemed in good condition. At that time it was the belief of the physicians that the tumor was doubtless a fast-growing sarcoma of the kidney, superinduced or accelerated by the injury. The abdomen continued to be distended, and breathing continued shallow. Shortly before 9 o'clock it was evident that the patient was becoming worse; the breathing

became more and more labored. The pulse increased enormously in rapidity until with the stethoscope its rate was so great, over 200 per minute, that it could not be definitely counted. The violent action of the heart then suddenly stopped, a few more pulsations occurred, and death took place at 9.

Postmortem Findings.—An hour later the wound was examined. At this time still another change had taken place. The sac of the kidney capsule was practically empty. The liver was back in its usual position, and was found to be entirely normal. There was no subphrenic exudate of blood, nor was there an abscess cavity in any place. The right kidney, too, was found in its normal position and, save for a slight loss of cortical tissue over an area an inch in diameter, was entirely normal. The ureter was not injured, save by stretching, and it was evident that this organ, as well as the liver, had been crowded to the left of the median line by the steadily increasing intracapsular hemorrhage. The examination of the kidney capsule showed a bruised and contused area at a spot immediately entad of the localized point of tenderness of which the child had complained. Three or four parallel lines of abrasion an inch long and a quarter inch apart were still visible on the outer surface of the capsule,

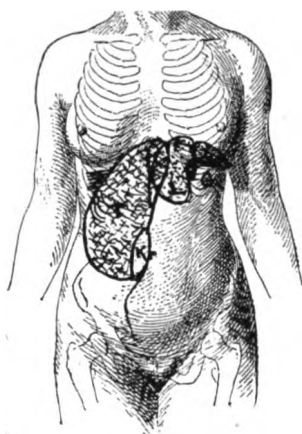


Fig. 2.—Relation of tumor (intracapsular renal hematoma) found at operation. T, tumor; K, kidney; L, liver; G, gallbladder.

and at this point it was evident that the capsule had been separated from the kidney cortex causing a small amount of intracapsular hemorrhage. Little by little this hemorrhage, in part, at least, arterial in character, had steadily continued and little by little the capsule had been separated from the cortex of the kidney and the cephalic pole of the capsule pushed upward behind the liver, following the curve of the diaphragm until at the end of a month the entire liver had been displaced to the left by the enormous intracapsular hematoma. The kidney itself had also been displaced in a similar way, and as its capsule had separated over practically the entire outer portion of the cortex, the kidney had been slowly displaced to the left of the median line taking with it the renal vessels and the ureter. The surgeon's finger, therefore, could reach easily to the vertebral column, and on the mesial side of the encapsulated mass only a small denuded area of the kidney could be felt. A thin section of the kidney cortex was undoubtedly pulled away here and there by the slow process of separation, and these sections of tissue deprived of their normal blood supply gave rise to the thin masses of tissue so much resembling a sarcoma in appearance which was noted at the operation.

As a result of the restitution of the kidney and of the liver to their normal position, after the collapse of the kidney capsule by the evacuation of its

pultaceous contents, the stomach and intestines released from long-continued pressure dilated materially, and this acute dilatation of the stomach, due to mechanical causes, was an undoubted factor in the sudden death of the child, since this pressure was exerted directly toward the heart and served to irritate and stimulate that organ to an enormous rate of pulsation.

DISCUSSION

It is at once apparent when the history of this unusual accident and sad sequence is considered in full detail, that we had from the very first to deal with a condition at once unusual in character and quite out of the realm of ordinary experience. The entire absence of all kidney symptoms which usually are indicated through the urine in cases of fracture of the kidney appeared to eliminate this organ as an important factor in diagnosis. The diagnosis of hematoma made at the first consultation and confirmed at the last one was correct, but the exact location of the extravasated blood was not determined at first, and was with difficulty determined even after death. The fact that the abdominal injury was due to blunt force made it possible for the capsule of the kidney to be severely bruised, but not cut through. The tumor caused by the escaping blood was small at first, firmly encapsuled and was concealed by its position beneath the costal cartilage. Its progressive increase due to hemorrhage from minute arterioles in the cortex of the kidney which did not or could not contract in the ordinary way, confined the blood within a capsule at once firm and elastic. Prevented by the pelvic brim from extending downward, the growth of the enlarging capsule followed along the diaphragmatic arch and steadily crowded the liver to the left, far out of its normal position. The median line of the pelvis of the kidney formed the sharp edge which during the process of growth and distention of the capsule so closely simulated the edge of the liver that at the time of the last consultation this sharp edge was believed by all of us to be the free edge of the liver crowded downward from the direction of the diaphragm.

Altogether the progress of the patient, the clinical history and the physical signs from time to time were misleading in many ways. They are here presented in the hope that in case a similar injury should occur to some other child they may be of assistance to others in determining earlier surgical interference.

59 West Fifty-Fourth Street.

PROGRESS IN PEDIATRICS

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF CHILDHOOD *

JAMES B. HOLMES, M.D.

BALTIMORE

The relations of the fissures of the lungs in infants have been made the subject of a study by Gittings, Fetterolf and Mitchell.¹ Nothing in reference to the course of these is found in standard textbooks and recent periodical literature. On the other hand, there are numerous references pertaining to adults. The authors have felt that carefully selected data would be valuable for comparison with similar relations as they exist in the adult, and a stimulus toward greater accuracy in clinical diagnosis. They cite references to show that anomalous fissures occur quite frequently, that there are at times variations in the normal fissures, and that the course of the oblique fissures in adults is far from constant.

The study is based on dissections of formaldehyd-hardened bodies of fourteen infants, ranging from 6 weeks to 14 months of age. The authors describe carefully the course of the fissures and find that differences between the fissures in adults and infants are slight and unimportant. Equally marked variations in the points of origin, course, and terminations are seen in both. Apparently these variations are not related to anatomic characteristics of the chest. It would appear that change in the shape of the chest goes *pari passu* with development of the lung, with the result that the relation of fissure to rib or to interspace remains practically unchanged. Variations in the fissures, therefore, cannot be predicted from anatomic characteristics of the chest.

Clinically, because the lower level of the lungs in infants, and probably in young children, does not extend quite so low as in adults, great care should be exercised to avoid damage to the diaphragm in performing thoracentesis. According to the authors, the sixth interspace in the midthoracic line and the seventh or possibly the eighth interspace in the line of angle of the scapula (at rest) represent the lowest limits of absolute safety for thoracentesis in early life.

* Submitted for publication Dec. 28, 1917.

1. Gittings, J. C., Fetterolf, A. G., and Mitchell, A. G.: A Study of the Topography of the Pulmonary Fissures and Lobes in Infants, *AM. JOUR. DIS. CHILD.*, 1916, **12**, 579.

PHYSIOLOGY

The mechanism of infants' suction has been further investigated by Michio Kasahara.² Auerbach, in 1888, divided suction into two kinds: (1) suction by inspiration, and (2) suction by the mouth, or the tongue. Suction by inspiration is made by the adult, and the necessary negative pressure in the mouth is caused chiefly by inspiratory action. Suction by the mouth is made by infants, and the negative pressure is due chiefly to the vertical diameter of the oral cavity being increased because the lower jaw is depressed. Auerbach held that suction by mouth does not give place to suction by inspiration until the child is 2 or 3 years old. There is difference of opinion as to the importance of the part played by the tongue in the action.

Kasahara used a Marey tambour and kymograph and registered the variations of pressure that occur within a nursing infant's bottle, in the form of regularly recurring curved lines, which he calls the curved lines of suction. Each cycle comprises a completed act of suction and swallowing, and its course may be divided into four parts, namely, (1) a descending part (meaning negative pressure) which represents the downward movements of the lower jaw bone, the oral cavity being extended in the vertical diameter, (2) a small elevation due to pressure on the nipple, (3) an ascending part (diminishing negative pressure) which Kasahara attributes to the running down of milk which has been taken into the mouth, and (4) a notch or concave curve, caused by swallowing.

Newly born infants produce irregular curves, with interruptions, or discontinuations, "for physiologic reasons." Healthy infants over a week old make curved lines of suction that are always regular and not discontinued. The presence of thrush, nasal catarrh, and the like, renders the curved line of suction irregular. Idiots are said always to make irregular curved lines of suction, probably because there are disorders in the coordination of muscles.

Benedict and Talbot,³ in a recent report from the laboratories of the Carnegie Institute, show that, contrary to the prevalent view, the human embryo is not born with a large store of carbohydrate. As a matter of fact it is only a few hours before whatever reserve of carbohydrate may have been present is exhausted, and the infant is thus thrown on its tissues (chiefly fat) for its energy supply. As colostrum does not fully meet the energy need of the first days, theoretically, at least, there is a possible danger of acidosis if the early noncarbohydrate

2. Kasahara, Michio: The Curved Line of Suction, *AM. JOUR. DIS. CHILD.*, 1916, **12**, 73.

3. Benedict, F. G., and Talbot, F. B.: The Physiology of the New-Born Infant, Pub. 233, Carnegie Inst. of Washington.

metabolism is overaccentuated. For this reason avoidance of undue muscular effort and excessive crying in the newly born infant is desirable. The practice of employing some form of artificial nourishment during the first days of the infant's life receives additional scientific support.

DEVELOPMENT

The heights and weights of New York City children from 14 to 16 years of age have been carefully studied by Frankel and Dublin⁴ for the Metropolitan Life Insurance Company. A state law requires that, before being employed in factories and the like, children shall have an employment certificate showing that they have completed the first six years of the school course and in the opinion of the examining officer have reached normal development for their age. This raises the question within just what limits a child may be considered to have reached normal development for his age.

Frankel and Dublin examined 10,043 children applying for certificates; 53.7% of these were boys. A number of interesting facts were brought forth in the study. It is found (1) that weight increases with height, exceptions being found only at extremes; (2) that girls are heavier than boys for any given height up to about 63 inches, beyond which height boys outweigh girls. (Bowditch had found 58 inches the dividing line.)

The average heights and weights were found to be as follows:

	14-15 Years		15-16 Years		Coefficient of Correlation Between Height and Weight
	Average Height, Inches	Average Weight, Pounds	Average Height, Inches	Average Weight, Pounds	
Boys	61.55	103.38	62.74	109.69	0.776 and 0.759
Girls	61.19	104.54	61.59	107.57	0.499 and 0.439

(Weights were taken in ordinary clothes. Bowditch found average weight of clothes to be: boys of 14, 8.09 pounds; of 15, 8.08 pounds; girls of 14, 7.54 pounds; of 15, 7.85 pounds.)

Both the heights and the weights of boys were found to be distributed over a greater range than those of girls. The interquartile range, that is, the limits which include the central 50 per cent. of cases is: 4.26 inches in height for boys and 3.05 inches for girls; 23.7 pounds in weight for boys and 19.83 pounds for girls. It is interesting to note that for the two-year period, 14 to 16 years, high school graduates were taller than boys and girls yet in the high school (boys, 0.18 inch; girls, 3.5 inches), and these in turn were taller than those in Grade 7 A (boys, 0.48 inch; girls, 0.62 inch). Also that the New York City boys and girls showed greater height (0.68 inch) and weight (5.03 pounds)

4. Frankel and Dublin: Heights and Weights of New York City Children, etc., Publication Metropolitan Life Ins. Co., New York, 1916.

than up-state boys and girls of like age and circumstances, and that they are *stockier*, that is, show greater weight per inch in height. Native-born Jewish boys and girls proved heavier than foreign-born ones, while Italian boys and girls were less tall and less heavy than those of foreign birth—conditions attributed to changed economic status of the parents.

As regards the range of variation that may be accepted as normal in granting certificates, the authors conclude: "A departure of 15 per cent. from the average weight for a given height is suggested as the limit below which children should be refused employment certificates, even if the medical examiner pronounces them well in other regards. In no case should a certificate be granted to a child whose weight is less than 70 pounds."

NUTRITION

Harold L. Higgins,⁵ in reporting from the Nutrition Laboratory of the Carnegie Institution a study on the rapidity with which alcohol and some sugars may serve as nutriment, says that alcohol has been commonly considered the most quickly available nutrient, and that it is, indeed, quickly absorbed. Just how quickly it displaces in whole or in part other nutrients that are burned in the body, that is, how soon it is oxidized, may be determined by observations on the respiratory quotient of the individual. In examining this it is found that the time elapsing between the taking of alcohol and the beginning of combustion varies with different (normal) subjects; it ranges from four to seven minutes in some subjects, up to ten to fifteen minutes in others.

Comparative observations made on normal subjects who received 100 gm. of sugar made up with water and cereal coffee to 300 c.c. volume, followed by 25 to 50 c.c. of water to clear the mouth, showed clearly that certain sugars when thus taken are burned quite as rapidly as alcohol. Alcohol begins to be burned in appreciable quantity in from five to eleven minutes after ingestion. Sucrose, lactose, levulose, begin to be burned quite as soon as alcohol, if not sooner. Glucose and maltose are utilized more slowly, approximately 20 to 30 minutes elapsing before their combustion comes to play an important part.

The entry of the United States into the world war has precipitated a large number of articles and books on the relation of available food supply to nutrition. It is not proper to review these in this place, but reference should be made in passing to one of the earlier books of this character to appear, that by Professor Mendel⁶ of Yale University.

5. Higgins, Harold L.: Rapidity with Which Alcohol and Some Sugars May Serve as Nutrient, *Am. Jour. Physiol.*, 1916, **41**, 258.

6. Mendel, Lafayette B.: *Changes in the Food Supply and Their Relation to Nutrition*, Yale Press, 1916.

Dr. Mendel's paper includes a study of the earlier food situation in Germany and refers to the work on wartime food supplies, by Eltzbacher, Oppenheimer, Rubner, Zuntz, and others.

In order that one foodstuff may be substituted for another it is necessary that it shall offer sufficient amount of available energy as expressed in calories, that it shall be digestible in the form in which it is used, that the proportions of protein, carbohydrate and fat shall be suitable, and that certain poorly defined elements called vitamins shall be present. Other factors, such as the palatability of the food, enter into consideration. Recent work by McCollum,⁷ and his collaborators, has shown that in the case of fats another hitherto unrecognized element must enter into consideration.

McCollum and Davis⁸ pointed out in 1913, that certain fats of animal origin contain a substance the nature of which is as yet unknown, which is essential for growth or for long continued maintenance of health of the rat. This indispensable factor, termed "the fat soluble A," has been shown to be not present in olive oil, lard and almond oil.

Further studies by McCollum, Simmonds and Pitz⁷ indicate that it is in general not present in fats and oils of vegetable origin, for example, in wheat oil, linseed oil, soy bean oil, and cottonseed oil. Corn, wheat and oats, and probably other grains supply this factor, but in insufficient amounts. Continued deprivation of this element lowers the bodily resistance of experimental animals.

Butter and the yolk of eggs contain this essential nutritional element in largest quantity. It is notable that cod liver oil contains it also (Osborne and Mendel).

CALCIUM IN BLOOD, URINE AND MILK

Henry Lyman⁹ has determined the amount of calcium present in the blood of twelve normal and forty-two pathologic persons [adults?] of both sexes. The determinations were made according to a new method¹⁰ and about 20 c.c. of blood was drawn in each case. The chief point brought out by this study seems to be that calcium content of the blood varies but little in the great majority of subjects. The averages for the males, with the exception of one who showed an unexplained and extremely low figure, was 6.1 mg. of calcium per 100 c.c. of blood, and for the females, 7.1 mg. One healthy young woman,

7. McCollum, E. V., Simmonds, N., and Pitz, W.: The Distribution in Plants of the Fat Soluble A, the Dietary Essential of Butterfat, *Am. Jour. Physiol.*, 1916, **41**, 361.

8. McCollum and Davis: *Jour. Biol. Chem.*, 1913, **15**, 167.

9. Lyman, Henry: The Calcium Content of Human Blood, *Jour. Biol. Chem.*, 1917, **30**, 1.

10. Lyman, H.: *Jour. Biol. Chem.*, 1917, **29**, 169.

whose history afforded no clue to the high result, gave readings of 9.6 mg. per hundred cubic centimeters.

The hope is expressed that these figures may help to establish a base line for further study of the metabolism of calcium.

A study of the calcium output in four healthy men and a healthy boy (aged 13 years) has been made by Nelson and Williams.¹¹ The urinary and fecal output was measured in each case over a period of five days. The subjects were not restricted in their diet in any way. The examinations were repeated after an interval of six months. The authors point out that most previous studies have come from equilibrium experiments, in which the subjects were on more or less restricted or abnormal diets. It is necessary to have sufficient data on normal behavior of the body with which to compare the findings in osteomalacia, osteoporosis, rickets, infantilism, and one might add, tetany.

From the data presented it appears that the average daily output of calcium in urine and feces varies in normal persons from 0.420 to 1.016 gm. (CaO 0.588 to 1.42 gm.) on unrestricted diet. In the same person the daily variation of unrestricted diet seems to vary between 15 and 25 per cent. As between the urine and the feces, the division averaged as follows: urinary excretion, 0.1754 to 0.6186 gm. of CaO; fecal excretion, 0.4125 to 0.8010 gm.; total daily excretion, 0.5879 to 1.4196 gm. Theoretically, at least the relative acidity or alkalinity of the urine should affect the proportion of calcium leaving the body through this channel. Some data on this point are recorded. There is need of further observations along these lines.

In a study on the relative amounts of calcium and magnesium excreted in the normal urine Nelson and Burns¹² conclude that in the normal individual either calcium or magnesium may be excreted by way of the urine in the larger amount, and that whichever element predominates does so constantly, or very nearly so, in that individual, and appears to be independent of the character of the food ingested. These authors think it probable that there is a selective action for calcium and magnesium on the part of the renal epithelium.

Of the twenty-five specimens examined there were seventeen in which calcium was excreted in larger amounts than magnesium. This is contrary to the findings of Hammarsten, who says, that of a daily urinary excretion of somewhat more than 1 gm., two thirds is magnesium and one third calcium. Twenty-two of the persons studied

11. Nelson, C. Ferdinand, and Williams, J. L.: The Urinary and Fecal Output of Calcium in Normal Men, Together with Observations on the Hydrogen-Ion Concentration of Urine and Feces, *Jour. Biol. Chem.*, 1916, **28**, 231.

12. Nelson, C. Ferdinand, and Burns, W. E.: The Calcium and Magnesium Content of Normal Urine, *Jour. Biol. Chem.*, 1916, **28**, 237.

were apparently normal university students, and the duration of the study would seem to exclude the possibility of the constant preponderance of magnesium being due to a sameness of diet.

The chemical changes produced in milk by the addition of lime-water have been studied by Bosworth and Bowditch.¹³ The custom of adding limewater to milk for infant feeding is an old one, and is based in part on the erroneous assumption that cow's milk is much more acid than human milk and requires neutralization. Bosworth and Bowditch find that the addition of limewater to milk, which normally contains some insoluble dicalcium phosphate, results in the precipitation of more calcium phosphate, the insoluble phosphates under these conditions being a mixture of dicalcium and tricalcium phosphates, CaHPO_4 and $\text{Ca}_3\text{P}_2\text{O}_8$; that it brings the serum of the milk towards the neutral point, the soluble alkalinity of the limewater being used up in the precipitation of the insoluble calcium phosphates above mentioned; and finally, that when milk to be used for infant feeding is treated with limewater and then diluted to such an extent that it has twice the volume of the original milk, or more, the soluble calcium and phosphorus may be reduced to amounts less than those which are present in human milk.

PHENOL AND CREATININ

Charles W. Moore¹⁴ has employed the Folin and Denis method of determining phenol in the urine to investigate anew the occurrence of phenol in the urine of infants. Several phenols are recognized as occurring in normal urine, phenol, paracresol, orthocresol, pyrocatechin, hydroquinone, and para-oxybenzoic acid. Of these, paracresol is thought to be the most important. Phenol found in the urine has been considered a product of bacterial activity in the intestine (Schild-Ellinger), but Blumenthal and Lewin claim that it is, in part at least, a product of endogenous metabolism.

H. Senator long ago found traces of phenol present in the urine of infants. In 1905, Ludwig F. Meyer, using the method of Kossler and Penny, found it present in the urine of seven infants, in amounts varying from 2.5 to 16.9 mg., and absent in none. The average for breast fed infants was 4.19 mg. and for artificially fed infants, 13.28 mg. No similar estimations appear to have been made since then.

According to Moore, breast fed infants show a phenol excretion of 5 mg. per kilogram of body weight, and artificially fed infants 8 mg.

13. Bosworth, A. W., and Bowditch, H. I.: The Chemical Changes by the Addition of Lime Water to Milk, *Jour. Biol. Chem.*, 1917, **28**, 431.

14. Moore, C. W.: The Phenol Excretion in the Urine of Infants, Including the New-Born, *Am. Jour. Dis. Child.*, 1917, **13**, 15.

The excess of phenol in artificially fed infants was ascribed by P. Mayer to decomposition in those fed on cow's milk, allowing the formation of more phenol than in those fed on breast milk. But Folin and Denis have shown that in adults, increasing the protein ingestion increases the phenol output; trebling the protein doubles the phenol, a rule that Moore finds applies also to infants. It seemed possible, since liquor amnii and meconium have been found negative for phenol (Senator), that light might be thrown on the question of an endogenous origin for phenol in the urine by examining the urine of starving new-born infants for this substance. Nineteen such infants were studied, and phenol was found present in every case, in amounts varying from 2.1 to 23.4 mg., an excretion of approximately 3.4 mg. per kilogram of body weight. The average total phenol excretion for the first three days of life was 11.2 mg., of which 76 per cent. was free and 24 per cent. conjugated. Moore concludes that as phenol was present during this period of starvation it must originate in part through endogenous metabolism.

Mention was made a year ago¹⁵ of Taylor's studies on the occurrence of creatinin and creatin in the urine of children. Taylor found that the sum of the creatin plus the creatinin in the urine of children compares approximately with the sum of the two constituents in the adult when due allowance is made for the weights of the individuals and the probable amounts of muscular tissues. He thought his findings might reasonably be ascribed to an incomplete conversion of creatin into creatinin by the developing organism. Veeder and Johnston¹⁶ have since studied the content of the blood of children in creatinin and creatin. They say that tables from Folin show in a general way that the blood of adults averages about 10 mg. of creatin per 100 c.c., with apparently no relationship between the amount of creatin and that of creatinin. Veeder and Johnston found less creatinin (rarely over 5 mg. per 100 c.c.) in the blood of children than in adults, and the total creatin-creatinin content rarely over 6 mg. (their patients were not all normal).

They could find no specific relationship in their figures between the creatinin and the creatin, nor any between the total amount of creatin and the clinical condition of the child. They found also no definite relation between the total nonprotein nitrogen and the creatin-creatinin content. They feel that retention of creatinin is merely part of general retention of nitrogenous substances in the blood and that

15. Holmes, J. B.: *Recent Work in Anatomy, Physiology and Pathology of Childhood*, *AM. JOUR. DIS. CHILD.*, 1917, **13**, 187.

16. Veeder, B. A., and Johnston, M. R.: *The Creatinin and Creatin Content of the Blood of Children*, *AM. JOUR. DIS. CHILD.*, 1916, **12**, 136.

there is no evidence at hand leading one to consider it a more delicate index of retention than any of the other nitrogenous substances; in fact, it seems to be more easily excreted.

PATHOLOGY

TUBERCULOSIS AND SYPHILIS

F. Parkes Weber¹⁷ contributes a lengthy survey of recent work on the problem of congenital infection with tuberculosis. The paper is accompanied by a long and, for the most part, quite recent bibliography. While the paper itself does not admit of abstracting, certain views expressed by the author may be mentioned here.

Genuine cases of congenital tuberculosis in human beings are undoubtedly very rare. There is no proof of paternal transmission, that is, through the semen (Sitzenfrey, 1909); and the extreme rarity of *primary* genital tuberculosis in vagina or uterus seems clinical evidence that direct paternal bacillary transmission practically does not exist (Knopf).

There are probably different ways in which the tubercle bacilli can pass from the mother to the fetus — late congenital infection. In the first undoubted case of congenital (fetal) tuberculosis, Schmorl and Birch-Hirschfeld (1891) suggested that the tuberculous infection did not occur until shortly before the death of the seven-month fetus (in cesarean section, directly after the death of the mother). Slight microscopic changes were detected only in the liver, and bacilli were present in blood films from the umbilical vein. Honjio (1909) described a case of human congenital tuberculosis in a five-month's fetus; there were enlarged and tuberculous retroperitoneal lymph glands. Dufour and Thiers (1913) recorded a case in the third to fourth month of pregnancy; the placenta appeared to be healthy, but the peritoneum of the fetus contained fluid which on animal inoculation gave rise to tuberculosis. Birch-Hirschfeld suggested that the organisms pass from the maternal to the fetal circulation by lodging in the placenta and then "growing through" the placenta into the fetal circulation, a view suggested to him from his observations in cases of anthrax. A. Gärtner (1893) explained the likelihood of a tuberculous lesion in the placenta being ruptured during some stage of labor with discharge of bacilli into the fetal circulation, and Rietschel (1909) in the case of an infant who was removed at birth from a tuberculous mother but developed clinical signs of tuberculosis and died, after three months, from generalized tuberculosis, suggested that the child might have escaped infection until the actual onset of uterine contractions.

17. Weber, F. Parkes: Congenital Tuberculosis—a Survey, *Brit. Jour. Child. Dis.*, 1916, **13**, 321.

Other methods of fetal infection suggested (Sitzenfrey) are that the chronic engorgement of villous capillaries might lead to their rupture into the maternal intravillous spaces, and that lowering of the blood pressure in the villous tufts might permit the entrance of maternal blood with transference to the fetal circulation of any bacilli free at that time in the maternal bloodstream. And, second, that tuberculous foci, localized in the decidua vera, might penetrate the amnion, infect the liquor amnii and thus give rise to intra-uterine infection of the fetus.

It has been shown that tubercle bacilli may be frequently demonstrated in the placentae of tuberculous women by the antiformin method, and this even when the mother's known clinical lesion is very slight (Novak and Ranzel, 1910). Apparently placental tuberculosis does not occur until the fourth month of pregnancy.

Pêhu and Chailer (1915) consider fifty-one published cases of congenital tuberculosis as conclusively genuine. In the infected fetus or infant there are generally well marked tuberculous lesions to be seen in the organs; but in some cases no pathologic-anatomic changes are found, though virulent tubercle bacilli are present in the fetal blood. Cases of the latter type may well have been infected intrapartum.

Parkes Weber concludes by saying it seems we may well suppose that occasionally a mother with some form of chronic, and perhaps even latent, tuberculosis may suffer from a temporary condition of "bacillemia" during pregnancy without succumbing; "for, probably, conditions of temporary tuberculous 'bacillemia' are not exceedingly rare in subjects of chronic tuberculosis, apart from pregnancy."

Eugene L. Opie¹⁸ has studied the occurrence of tuberculous lesions in children and adults in St. Louis, as shown in the necropsy room. It is well known that first infection in animals commonly spreads rapidly to the regional lymph nodes and produces in them a caseous lesion that far exceeds in extent the lesion at the original focus. In animals that have already been infected, a second infection, as Koch showed years ago, shows greater tendency to heal and does not extend to regional lymph nodes. This observation, says Opie, has been confirmed by numerous observers. It is from this point of view that the lesions found in the present series are studied.

The series comprises twenty-two cases of tuberculous infection in children from 0 to 18 years of age, and about twice this number of adults. The actual conditions found are shown in the accompanying table. The presence of lesions was sought by taking roentgenograms of the lungs and appendages and then, by subjecting them to careful

18. Opie, Eugene L.: The Focal Pulmonary Tuberculosis of Children and Adults, *Jour. Exper. Med.*, 1917, **25**, 855.

gross examination, dividing them where necessary into sections from 0.5 to 1 cm. in thickness, and supplementing this with microscopic examination.

The accompanying table shows that the conditions found in the postmortem examination of adults in St. Louis accords well with those found by Naegeli in Zurich, and by Burkhardt in a far larger number of necropsies in Dresden. (The adult material appears to have come from the Barnes Hospital in St. Louis; it is not clear from what social strata the patients came.)

OCCURRENCE OF TUBERCULOUS LESIONS IN CHILDREN AND ADULTS IN ST. LOUIS

Age, Years	Number of Necropsies	Tuberculosis				
		Present		Fatal	Nonfatal	In Those Who Have Died with Other Diseases, per Cent.
		Number	Per Cent.			
Children:						
Under 1	48	4	9.8	4	0	0
1 to 2	16	1	6.2	1	0	0
2 to 5	14	6	42.8	3	3	27.3
5 to 10	11	5	45.5	2	3	33.3
10 to 18	9	6	66.7	1	5	62.5
Adults:						
18 to 30	6	6	100.0	1	5	100.0
30 to 50	23	23	100.0	1	22	100.0
50 to 70	15	15	100.0	1	14	100.0
70+	6	6	100.0	0	6	100.0

A second table shows the relative frequency of active, encapsulated caseous, and healed tuberculosis. The tuberculous infection was regarded as healed only when all the lesions were firmly calcified and surrounded by fibrous tissue. "Healed tuberculosis" was found in no children under 5 years of age, in 18 per cent. of those (11) between 5 and 10 years of age, in 11 per cent. of those (9) between 10 and 18 years, and in over one third of all adults examined. No encapsulated caseous lesions were found in children under 2 years of age (59 in all), but thereafter the percentage of encapsulated caseous lesions rose rapidly toward 50 per cent., the percentage found in adult bodies. The percentage of active tuberculosis was relatively low under 2 years of age, 6 to 9 per cent., rose to 35.7 per cent. between 2 and 5, then fell to 18 per cent. between 5 and 10 years, 11 per cent. between 10 and 18 years, and then rose to 13 to 16 per cent. for adult life. The value of these figures suffers from the small number of bodies examined in some age periods.

From his study of the individual lesions the author concludes that tuberculosis of children does not select the apices of the lungs, is accompanied by massive tuberculosis of regional lymphatic nodes, and exhibits the characters of tuberculosis in a freshly infected animal. He holds that tuberculous infection is practically universal. His tables show no encapsulated or healed lesions before the third year of life. Thereafter there is a steady increase in the percentage of cases showing capsulated caseous lesions, until in adult life 50 per cent. of all the individuals examined show them. Accompanying this is a slower but steady rise in the percentage of bodies showing "healed tuberculosis," until in the adult bodies one third showed only firmly calcified and completely healed pulmonary and lymphatic lesions.

The circumscribed tuberculous foci which occur in the lungs of adults do not differ in character and distribution from those which are found in older children. They rarely exceed 1 cm. in diameter and the smaller nodules, perhaps not more than 1 mm. across, are found with much difficulty even when they are calcified and cast a conspicuous shadow on the roentgen-ray plate. Attention is often first attracted to these pulmonary nodules by the more conspicuous lesions almost always present in the regional lymphatic nodes.

In contrast with this, the tuberculosis which occurs in the pulmonary apices of adults (clinical "tuberculosis" of adults) has the character of a second infection. It is similar to the usual or fatal phthisis and unaccompanied by caseation of the regional lymphatic nodes.

The article is illustrated by numerous diagrams showing the actual location of the lesions in individual cases and by reproduction of the roentgenograms.

A. Filia¹⁹ describes the renal lesions found by him in the body of a 7-year-old tuberculous boy. He deals particularly with the mode of formation of giant cells in the glomeruli. The question is an old one, and most of the references given date from the seventies and early eighties. The literature of the subject was collected by Kostnitsch and Wolkow in 1892. The question at issue is whether the giant cells found in the glomerular tufts in renal tuberculosis are derived from the connective tissue elements of the blood vessels, etc., or whether they are formed as a syncytial fusion of the epithelial cells. To Professor Filia, who is director of the pediatric clinic of the University of Sasaari, the process appears to be a true transformation on the part of the vascular and epithelial cells; that is, of the whole interior of the glomerulus, into a large syncytial giant cell, which is limited by the normal epithelium of the capsule. He does not find just this transfor-

19. Filia, A.: Intorno alla formazione delle cellule giganti dai glomeruli nella tubercolosi renale, *La Pediatria*, 1916, **24**, 705.

mation described by the older authors. He regards it as due to the direct action of tubercle bacilli that have been carried into the glomerular tufts, as seen in experimental animals, and not to extension of the process from connective tissue elements.

THYMUS

Jean Oliver²⁰ describes the histopathological findings in the thymus of a 6-weeks-old congenital syphilitic. Numerous cysts were present. Cysts in the thymus of the new-born who were first described by Cruveilhier in 1829, and carefully studied by Dubois in 1850. Dubois regarded the formations as abscesses, and they have since been called "Dubois abscesses." With the introduction of microscopic study Chiari, in 1894, showed the supposed abscesses were in reality cystic spaces lined with a definite epithelial covering of a flat stratified type. He described these cysts as arising from the Hassall bodies by a process of degeneration, an ingrowth of small thymic lymphocytes.

Apparently only eight cases of true cystic thymuses in infants have since been described. The present report contains reproductions of the microscopic appearances of the thymus. As the result of his study the author concludes that syphilitic disease of the thymus in infants is manifested primarily by a degeneration of the lymphocytes and Hassall's bodies, with a hypertrophy of the reticular epithelium and hyperregeneration of the concentric corpuscles. The process may give rise to the formation of cystic cavities by dilatation and fusion of the degenerating Hassall bodies.

ESOPHAGUS AND TRACHEA

Edmund Cautley²¹ describes the postmortem findings in a case of congenital malformation of the tracheo-esophageal septum in a 5-day old infant, and reviews the various known forms of malformations of the esophagus. He considers the condition rare and quotes Shukowsky as seeing only one in 50,000 newly born infants; though, on the other hand, seven occurred in a Copenhagen lying-in hospital in sixteen years.

Malformations of this region may be subdivided into various groups as follows: (1) *complete absence*, generally associated with gross malformations, as in monsters; 8 cases on record; (2) *double esophagus*, with reunion at the lower end; 2 published cases; (3) *diverticula* or *pouches*, pharyngeal rather than esophageal, being situated posteriorly at the junction of the pharynx and esophagus; (4) cysts arising during

20. Oliver, Jean: Syphilitic Disease of the Thymus in Infants and the Mode of Origin of the Dubois Abscesses, *AM. JOUR. DIS. CHILD.*, 1917, **12**, 158.

21. Cautley, Edmund: Malformations of the Esophagus, *Brit. Jour. Child. Dis.*, 1917, **14**, 1.

separation of the trachea from the esophagus and probably from fetal outgrowths of the esophagus; (5) *tracheo-esophageal fistula* without other abnormality—apparently only 6 on record; (6) *congenital dilatation*, occurring usually after infancy, and in most instances secondary to spasm or stricture, though sometimes apparently dependent on congenital atony or defect of the wall and possibly analogous to congenital dilatation and hypertrophy of the large intestine; (7) *atresia without fistulous communication with the trachea* in various types; about 50 cases reported, and (8) *atresia, with the lower end of the esophagus opening into the trachea, and very rarely into a bronchus*, the common type, of which about 85 have been reported.

Atresia without fistulous communication with the trachea, Group 7, appears as (a) atresia or stricture occurring as an upper esophageal sphincter (House) or at the level of the cricoid cartilage (House), or an inch above the diaphragm (Bertram Rogers, Dun), or an inch above the cardiac end of the stomach (Whipham and Fagge), and so on; as (b) *upper part normal, or forming a culdesac, and the lower portion forming a fibrous cord or more or less completely obliterated*; and as (c) *nonobliteration of the lumen and union of the two ends by a cord or band*. Of these three subtypes, those designated (a) and (b) are the more common; about thirty (some of them not truly congenital) and twenty cases, respectively, having been reported.

The anatomic conditions and various views as to the mode of development of these varied malformations are described by Shattock, Dickie and Keith (1910) among others.

Barton²² has described the condition of the larynx and trachea in stillborn infants and its bearing on artificial respiration.

HEART AND GREAT VESSELS

Gauss²³ reports a case of congenital atresia of the aorta. The condition was found in a routine postmortem examination of a male infant who died on the third day. The child had appeared normal.

At necropsy there was found a congenital atresia of the aorta at the orifice, total absence of the aortic valves, and a common opening for the coronary arteries into the left ventricular cavity. There were also hypertrophy of the left ventricular wall, dilatation of the right ventricle, passive congestion of the viscera and other lesions.

It is suggested that during the first days of life blood from the superior vena cava followed the same course as in the normal fetal

22. Barton, E. A.: The Condition of the Larynx and Trachea in the Still-born Infant and Its Bearing on Artificial Respiration, *Jour. Obst. and Gynec. of Brit. Emp.*, May, 1915, p. 138; *Abstr., Arch. Pediat.*, 1916, **33**, 469.

23. Gauss, Harry: Congenital Obliteration of the Aorta, *AM. JOUR. DIS. CHILD.*, 1916, **12**, 606.

circulation; that that from the inferior vena cava entered the right auricle, passed through the foramen, and entered in whole or in part the left ventricle where it was forced back through the foramen ovale into the right auricle, whence it went with the blood from the superior vena cava into the right ventricle, then into the pulmonary artery, where it divided, part going into the pulmonary circulation and the remainder into the aorta through the ductus arteriosus; and, finally, that blood returning from the pulmonary circulation into the left auricle was forced by contraction of the left ventricle through the foramen ovale into the right auricle where it mixed with the other blood. Such a circulation could be successfully continued as long as the right ventricle remained capable of serving both the pulmonary and the systemic systems, and offered at least a possible explanation.

Congenital obliteration of the aorta occurs in two main forms: (1) closure at the orifice (as mentioned), and (2) closure at the isthmus. The latter form is known as coarctation of the aorta and is much the more frequent anomaly. Over 200 cases have been reported (Abbott); some of the persons have reached adult life (Hochsinger, Le Count). Atresia ostii aortae is less common, and patients usually do not live more than a few weeks. Rauchfuss collected twenty-four cases, and one infant is known to have lived twenty-seven weeks. Both forms are recognized as congenital malformations, or developmental anomalies, though an inflammatory origin has been postulated.

Hess²⁴ reports a case of congenital atresia of the right auriculo-ventricular orifice with complete absence of the tricuspid valves. Such cases are rare. To make the anomaly compatible with life it is necessary that there be a patent foramen ovale or at least an opening in the interauricular septum and that the two ventricles communicate. There may also be a patent ductus arteriosus. Such cases are spoken of as uncomplicated, or simple cases of tricuspid atresia. When further anomalies, such as transposition of vessels co-exist, the cases are called complicated.

The case here reported is an uncomplicated case, and the patient lived to 1 year of age. Of the eight other recorded uncomplicated cases, only one lived beyond a year.

In the present instance necropsy showed the body of the heart to be comprised of a greatly hypertrophied left ventricle. The left auricle was also enlarged; the right auricle was prominent; the foramen ovale was large and open. The tricuspid orifice and tricuspid valve were absent, there being nothing to mark the place where they should be.

24. Hess, Julius H.: Congenital Atresia of the Right Auriculoventricular Orifice with Complete Absence of Tricuspid Valves, *AM. JOUR. DIS. CHILD.*, 1917, **13**, 167.

The interventricular septum was perforated by an opening one sixteenth of an inch in diameter. The mitral orifice was dilated, the mitral valve was very large, and the papillary muscle of exceptional size. The ductus arteriosus was rather small, but patent. The relations of the great vessels were practically normal. The pulmonary artery showed no stenosis, though its branches were of smaller caliber than normally.

Hess pictures the circulation as follows:

All venous blood went from the right auricle into the left auricle, thence to the left ventricle, thence most of it into the aorta and systemic arteries. A small percentage (possibly about 20 per cent.) went through the interventricular foramen, into the right ventricle and thence into the pulmonary artery and lungs, and a very small percentage of this was shunted by the ductus arteriosus into the aorta.

The symptoms were those of dyspnea and cyanosis, clubbing of the fingers and toes, and venous congestion. There was enlargement of the heart and a wide mediastinal shadow as seen by the roentgenogram. Over the base of the heart a long, loud systolic murmur was heard; it was thought to be best heard over the pulmonary region. No murmurs were heard at the apex.

In the diagnosis of tricuspid atresia the author attaches importance to the hearing of a loud systolic murmur having its point of maximum intensity at the base of the heart (sternum), the intensity diminishing from that part—the murmur of pulmonary stenosis, in contrast, being loudest and best heard in the second left intercostal space.

SYPHILITIC (?) SCLEROSIS OF LEFT VENTRICLE

F. Parkes Weber²⁵ reports a case of extensive fibrosis of the left ventricle in a 10-year-old boy of Russian Jewish parentage. The child was delicate looking and had suffered from repeated attacks of melena, slight hematemesis and hemoptysis. There was a history of an illness accompanied by the passage of blood per rectum two years previously. The heart was enlarged but presented no murmurs. The urine did not contain albumin. The child died four months later with symptoms suggestive of embolism of the right iliac.

Necropsy revealed a hypertrophied and dilated heart, weighing 12½ ounces. The myocardium of a large portion of the outer wall of the left ventricle had undergone a fibrous change and had been converted into hard, white, scarlike tissue. The great trunks of the coronary arteries were not stenosed. There was soft organized antemortem thrombus in the cavity of the left ventricle, and the right

25. Weber, F. Parkes: Extensive Fibrosis of the Left Ventricle in a Child, *Brit. Jour. Child. Dis.*, 1916, **13**, 289.

common iliac artery was occluded at its bifurcation by recent embolism. There was no valvular disease.

There was great thickening and atheromatous change in the abdominal aorta. "At one spot where there was an atheromatous deposit the muscular elastic coat was thin and bulging outward to form a kind of miliary aneurysm." Microscopic examination of the wall of the left ventricle showed that the small arteries were the seat of a marked endarteritis obliterans, which did not altogether obliterate their channels. The adjacent capillaries were much dilated, as if to establish a compensatory circulation, and immediately around these were well preserved cardiac muscle cells; elsewhere the muscle fibers had been replaced by connective tissue overgrowth. The change might be viewed as replacement fibrosis of ischemic origin.

The vascular changes were believed to be syphilitic in nature (congenital). Secondary thrombosis and embolism led to the child's death. His blood serum was not examined for the Wassermann reaction. There was a suggestive family history.

Morgan²⁶ reports a case of congenital dextrocardia, with patent foramen ovale; necropsy at 9 months.

Jägerskiöld²⁷ reports an instance of congenital rhabdomyoma of the heart.

Rous and Robertson,²⁸ in a series of experimental studies on normal animals, animals rendered plethoric by transfusion of blood, and anemic animals (hemorrhage), find that the fate of the red corpuscles in these species of animals is to be fragmented one by one, while still circulating, to a fine, hemoglobin-containing dust. The cell fragments are rapidly removed from the blood, apparently by the spleen, and, under exceptional conditions, by the bone marrow. Their ultimate fate remains to be discovered. They find also that the increased destruction of red cells in animals rendered plethoric by transfusion takes place predominately by a fragmentation of the corpuscles without loss of hemoglobin; also that the microcytes and poikilocytes observed in animals, with a severe anemia due to hemorrhage, are not put forth as such by the bone marrow, but are portions of cells fragmented while circulating, as earlier asserted by Ehrlich.

Rous and Robertson say:

The cells thus fragmented are for the most those new formed to meet the exigencies of the situation. Such cells are in a large part unable to withstand the wear and tear of function. There results a vicious cycle. The anemia

26. Morgan, H. J.: Dextrocardia, Congenital, with Patent Ductus Ovale. Necropsy at Nine Months, *AM. JOUR. DIS. CHILD.*, 1916, **12**, 233.

27. Jägerskiöld, E. H., Rhabdomyoma of the Heart, *Finska Läk. sällsk. handl.*, 1916, **58**, 953.

28. Rous, Peyton, and Robertson, Oswald H.: The Normal Fate of Erythrocytes. I. The Findings in Healthy Animals. II. Blood Destruction in Plethoric Animals with Simple Anemia, *Jour. Exper. Med.*, 1917, **25**, 651 and 665.

renders the bone marrow unable to put forth proper cells, and those it does produce are soon destroyed, thus prolonging the condition. A similar state of affairs probably exists in many human anemias.

The microcytes and poikilocytes, fragments, accumulate in the spleen, indicating that this organ exercises some important function in connection with them. Phagocytosis of red corpuscles, while frequent in the normal dog, rat and guinea-pig, is slight in man and certain other animals that are mentioned. Nothing is said to the final fate of the blood pigment; reference is made to the recent work of Whipple,²⁹ who proved that the bile pigments may have other sources than the blood.

Stillman,³⁰ in a study of three cases of von Jaksch's anemia, the patients aged 9 years, 8 months, and 18 months, respectively, describes the splenic pictures in detail and reviews some recent literature on the subject, including experiences with splenectomy. He defines von Jaksch's anemia as follows:

A condition occurring in children, marked by anemia, slight enlargement of the liver and marked enlargement of the spleen, and sometimes an enlargement of the superficial lymph nodes. The blood picture is characterized by a great diminution in the red cells and the hemoglobin and a persistent leukocytosis of varying degrees. Nucleated red cells are nearly always present, sometimes in large numbers, and occasionally myelocytes are seen. Most of the patients show a definite tendency to recovery, though a few die. In those who live, the abnormal blood picture may persist for a very long period of time though the patient is clinically well.

The condition is to be distinguished from that form of splenic anemia without leukocytosis, occurring in children (Wentworth and others). The occurrence of leukocytosis is one of the most important criteria of the disease, as insisted on by von Jaksch and supported by late authors. Usually it is for the most part a mononucleosis; sometimes the polynuclears predominate. The condition is associated often with rickets, and Marfan has gone so far as to say that the disease is rickets. Stillman thinks it is more logical to conclude, from the available evidence, that von Jaksch's anemia is due to the action of toxic or infectious agents which may or may not at the time produce rickets. The picture in the spleen is one of connective tissue increase, atrophy of the malpighian bodies and myeloid metaplasia; the atrophy of the follicles is apparently due to increase in the pulp elements rather than to connective tissue increase. Poikilocytosis and other evidence of rapid blood regeneration are present in the blood stream.

Stillman thinks the predominant activity of the spleen in these cases is a destructive one. He finds that splenectomy has been done

29. Whipple: *Am. Jour. Physiol.*, 1916, **40**, 349.

30. Stillman, Ralph G.: *A Study of von Jaksch's Anemia*, *Am. Jour. Med. Sc.*, 1917, **153**, 218.

in six cases, in five of which it was followed by apparently lasting improvement, and concludes that this form of treatment has a large place in the therapeutics of von Jaksch's anemia, though he adds it should not be adopted too hastily.

MYELOGENOUS LEUKEMIA IN AN INFANT

Knox³¹ reports a case of myelogenous leukemia in an infant. The symptoms were apparently referable to the gastro-intestinal tract. There was no demonstrable enlargement of the lymphatic glands or of the spleen and no evidence of hemorrhage or of necrosis of the mucous membrane. There were 200,000 white cells per cubic centimeter of circulating blood. The presence of a large number of myelocytes (from the bone marrow) suggested the foregoing diagnosis. The extreme youth of the patient (9 months) and the rapid course of the disease (less than three weeks) are noteworthy.

GASTRO-INTESTINAL TRACT

Intestinal Obstruction.—In a recent experimental study of acute intestinal obstruction, Dragstedt, Moorhead, and Burcky³² note that systemic bacterial invasion of the organism from the obstructed intestine does not occur (McKenna and others), and that the clinical and experimental evidence so far obtained points to quickly developing and rapidly fatal toxemia. They summarize the more important views regarding this toxemia as follows:

Hartwell, Hoguet, and Beeckman concluded from experiments on dogs that death in experimental intestinal obstruction is due, first, to a dehydration or loss of water from the tissues as a result of the excessive drain into the lumen of the intestine, and vomiting, and, second, to the presence of a toxin in the circulating blood. The toxin is believed to be normally present in the lumen of the intestine and the factor admitting this toxin into the blood is the damage to the intestinal mucosa. The life of the animal after experimental obstruction may be prolonged by the subcutaneous injection of normal saline solution.

Murphy and Brooks conclude from their experiments on dogs with experimental intestinal obstruction, that death is due to toxemia, independent of infection of the peritoneal cavity or the general circulation. The toxin is formed as a result of bacterial growth in the obstructed intestine. It is not absorbed through a normal mucosa, but gains entrance to the blood stream when the mucosa of the intestine has been damaged. They emphasize the significance of the abnormal absorption in the production of the symptoms.

Whipple, Stone and Bernheim believe that death in these cases of obstruction is due to the absorption directly into the blood of a perverted secretion of the duodenal or upper jejunal mucosa. They assume a disturbed physiologic balance of the mucosa by which abnormal products are formed and secreted

31. Knox, J. H. M., Jr.: Case of Acute Myelogenous Leukemia in an Infant, *AM. JOUR. DIS. CHILD.*, 1916, **11**, 462.

32. Dragstedt, Lester R., Moorhead, James J., and Burcky, Fred W.: Intestinal Obstruction. An Experimental Study of the Intoxication in Closed Intestinal Loops, *Jour. Exper. Med.*, 1917, **25**, 421.

into the blood stream. This perverted secretion is a highly toxic substance and they claim that it can be recovered from the lumen of the intestine in cases of obstruction. Some work has been reported on the chemical nature of this toxic substance, and attempts have been made to immunize dogs to it.

Draper believes that the cause of death in intestinal obstruction is due to an aberrant activity of the duodenal and probably the pancreatic cells. He appears to have forsaken the view taken by him several years ago of a normal toxic secretion from the duodenal mucosa which is neutralized by the secretions of the intestine lower down.

They note further that there has not been sufficiently further investigation of the chemical nature of the toxic substances found in the lumen of the intestine in cases of intestinal obstruction to determine whether they are essentially different from the toxic substance shown by Roger and Garnier to be present in the lumen of the normal stomach and intestine, and add that we should expect to find materials, in such a mixture of food substances and bacterial end-products as exits in the normal alimentary tract, which are toxic when injected into the blood stream. It is the function of the cells of the alimentary mucosa to charge substances in the lumen of the intestine to the substances which can enter the bloodstream without harm to the organism. Their normal action is both secretory and absorptive, and Braun and Boruttan have shown that absorption from the intestinal lumen is in reality decreased in cases of acute experimental obstruction.

The theory that under conditions of obstruction the normal physiology of the mucosa cells is so changed that they secrete a powerful toxin into the circulation does not seem probable to these authors, especially since in cases of congenital atresia of the intestine, though the secretions of the intestinal glands begin early in life, the infant shows no sign of toxemia or untoward effects until bacteria gain entrance to the alimentary tract after birth.

By washing out an isolated loop of the upper part of the jejunum with sterile water and ether the authors were able so to reduce the bacterial content of the loop that the remaining uninjured mucosal cells were able to take care of the rest. Dogs so treated quickly recovered from the immediate effects of the operation and did not show any subsequent ill effects though kept five months or longer.

From these and many other experiments, Dragstedt, Moorhead and Burcky conclude that closed intestinal loops from which bacteria are first removed are compatible with life; that closed intestinal loops in which bacteria are present but in which tissue necrosis is prevented, are compatible with life; and that closed aseptic intestinal loops in which the blood supply is completely occluded are compatible with life. Also, that the normal secretions and bacterial products of the duodenum and jejunum are not sufficiently toxic to produce any symptoms when allowed to drain into the abdominal cavity. And, finally,

that bacterial activity plus necrotic tissue, or the absorption of toxic products resulting from the action of putrefactive bacteria on necrotic tissue is the important factor in the rapid death in simple closed intestinal loops.

Just how far the conditions present in closed isolated unwashed loops of the intestine resemble those found in clinical obstruction seems problematic to these authors. They believe, however, that the symptoms and pathology of these simple closed loops resemble cases of acute obstruction in man in which there is an accompanying occlusion of the blood supply to a part of the intestine (volvulus, strangulated herniae, etc.).

Bile Circulation.—Hooper and Whipple,³³ in reporting a series of experimental studies on bile secretion in dogs, say that their results exclude the possibility of bile absorption from the intestine; that there is no evidence to support the theory of "bile pigment circulation"; and that their experiments give no support to Addis' theory of pigment conservation, urobilinogen absorption from the intestine and synthesis toward hemoglobin. It is suggested that urobilinogen may be formed in other body tissues rather than absorbed from the intestine.

Enlargement of the Colon.—Cadwallader³⁴ has reported a case of Hirschsprung's disease with complete bibliography to Jan. 1, 1916. Additional isolated cases of megacolon have been reported by C. A. Hamman (Cleveland Med. Jour., 1917, 16, 88); by B. Guttmann (New Jersey Med. Jour., 1916, 13, 629); also by R. de J. de Jong (Congenital Megacolon, Nederl. Tijdschr. v. Geneesk., 1916, 1, 1788).

New Growths.—Goodman³⁵ reports a case of lymphosarcoma of the sigmoid in a 4-year-old girl. She presented an irregular mass in the right umbilical and inguinal regions, which, on palpation, was found to be hard, irregular and nodular; which moved freely with respiration and felt very superficial. The mother had noticed this lump three weeks earlier, and there had been bleeding from the rectum. The child had previously become somewhat constipated and afterwards had severe abdominal pain. At one time as much as half a pint of pure blood was passed while straining at the stool. These attacks became more frequent and the child exhibited extreme pallor.

The tumor was not painful to the touch and with care could be moved from one side of the abdomen to the other. Two days later it

33. Hooper, C. W., and Whipple, C. H.: Bile Pigment Metabolism: The Influence of Fresh Bile Feeding on Whole Bile and Bile Pigment Secretion, *Am. Jour. Physiol.*, 1917, 42, 264.

34. Cadwallader, R.: A Case of Hirschsprung's Disease, with Bibliography to Jan. 1, 1916, *Arch. Pediat.*, 1916, 33, 665.

35. Goodman, A. L.: Lymphosarcoma of the Sigmoid, *Arch. Pediat.*, 1916, 33, 721.

remained in a transverse position across the abdomen, corresponding to the transverse colon. In a couple of days thereafter it had moved across to the left side of the abdomen just below the splenic flexure. The cervical, axillary and inguinal nodes were palpable.

The Wassermann and von Pirquet reactions were negative. The leukocyte count was 11,600; polynuclears, 62 per cent. There was no history of vomiting and the roentgen-ray examination revealed a distinct obstruction in the large intestine, apparently in the distal portion of the transverse colon. The character of the shadow was thought to suggest malignancy.

At operation a tumor of the sigmoid, 6 inches in length and 3 inches in width, was found, together with metastatic nodes in the mesentery. Resection and end-to-end anastomosis was performed. The child died a few days later of asthenia. The outer surface of the ovoid tumor mass was irregular, nodular, and soft. The lumen of the intestine passed through the mass eccentrically; the mucosa being replaced in part by an irregular, white, nodular tumor mass for the most part fairly clean, but in one area extensively ulcerated.

The microscopic examination showed the original structure to be almost entirely obliterated by a diffuse sarcomatous infiltration composed of closely packed small round cells, about the size of lymphocytes. There were no marked areas of necrosis. Mitotic figures were exceedingly abundant.

Such cases as the foregoing are not extremely rare, but are of sufficient importance to be reported. The clinical onset of the illness is always acute; the symptoms appearing with the slow growing tumor, which finally occludes the intestine.

The question of cancer of the various organs at different ages has been considered by F. Harbitz and E. Platon.³⁶

Frolich³⁷ reports the occurrence of cancer in a year old infant. The first symptoms were noticed in a healthy child at 9 months; the condition was confirmed by microscopic examination after an exploratory laparotomy, and proved fatal in five months. Frolich quotes Philipp's compilation of eighty-seven cases of cancer in children; twelve of which were instances of carcinoma of the liver, seven being in children under 10 years. Forty-six per cent. of the first mentioned series occurred in the digestive tract.

Adams³⁸ reports an instance of glandular carcinoma of the uterus in a child of 2½ years. For three weeks before admission to the hos-

36. Harbitz, F., and Platon, E.: *Norsk Mag. f. Lægevidensk.*, 1917, **78**, 145.

37. Frolich, R.: *Cancer in Liver of One Year Babe*, *Norsk Mag. f. Lægevidensk.*, 1917, **78**, 78; *Abstr. in Jour. Am. Med. Assn.*, 1917, **68**, 945.

38. Adams, Joseph E.: *Glandular Carcinoma of the Uterus in a Child Aged Two and a Half Years*, *Brit. Jour. Child. Dis.*, 1916, **13**, 266.

pital there had been a discharge of blood from the vagina. There was a palpable tumor in the hypogastrium, but no tenderness. On abdominal exploration the left retrovesical space was found to be occupied by a rounded cystic growth about half the size of a tennis ball and apparently attached to the roof of the vagina. It proved to be a cystic hemorrhagic mass and too adherent for complete removal. The bleeding reappeared and the child died two months later.

At necropsy the pelvic organs were removed in their entirety. A sagittal section showed both the body and the cervix of the uterus to be largely replaced by a necrotic growth, which had extended into the retro-uterine pouch and grown into the cavity of the vagina. The ovary and tube on each side was present and intact.

The tumor showed a network of supporting tissue and a number of areas where hemorrhage had obviously occurred. At one point a small portion of the growth was seen protruding through the inner wall of the bladder. Microscopically the growth proved to be a carcinoma with columnar and cuboidal cells having a somewhat tubular arrangement. Many of the tubules were provided with a capillary and a minimal amount of intervening connective tissue. There were many areas of degeneration, with loss of structure and irregular grouping of the cells. The growth appeared to fall into the group of carcinomas arising in the glandular epithelium of the body of the uterus. There was also caseating tuberculosis of the lungs and bronchial glands.

An instance of dermoid cyst of the ovary in a child of 5 years is reported by G. H. Cattermole.³⁹

The occurrence of a pancreatic cyst in a boy 8 years of age is reported by G. P. Shidler.⁴⁰

Reference was made last year to the occurrence of serous cysts of the mesentery in children as reported by a number of observers. An additional case is recorded by Montanari.⁴¹

CENTRAL NERVOUS SYSTEM

Schlapp and Gere⁴² report the clinical, postmortem and histopathologic findings in eight cases of internal hydrocephalus of the obstructive type, with especial reference to obliterating lesions of the aqueduct of Sylvius as the cause of the ventricular distention.

39. Colorado Med., 1917, **14**, 25.

40. Nebraska State Med. Jour., 1916, **1**, 35.

41. Montanari, U.: Di una cisti sierosa del mesentere, Rivista Osp., 1916, No. 12; Abstr. by S. Maggiore in La Pediatria, 1916, **24**, 748.

42. Schlapp, Max G., and Gere, Belden: Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus, AM. JOUR. DIS. CHILD., 1917, **13**, 461.

The recently published articles on the origin and absorption of spinal fluid by Weed and Wegefarth (introduction by Cushing), Frazier and Peet, Dandy and Blackfan, Dixon and Haliburton, and Hayes are referred to briefly. It is found that L. W. Weber (1906) in summing up the pathologic considerations in a number of cases, came to the conclusion, not greatly at variance with present day ideas, that three mechanical factors figure predominately in the production of hydrocephalus. These are (1) an increased fluid production due to inflammatory changes in the choroid plexus, the ependyma and brain substance, as well as obstructive processes in the choroidal vessels; (2) impediment to the outflow of the cerebrospinal fluid, via the venous and lymphatic channels, besides the obstacle of a frequently existing, chronic, diffuse leptomeningitis, causing an impermeability of the subarachnoid space; and (3) lessened resistance of the ventricular walls due to inflammatory, degenerative, or sclerotic processes in the affected areas. The last mentioned factor, that of diminished resistance, accounts for the cases coming on in later life where the dilatation of the ventricle may be symmetrical or confined to one ventricle, or to a portion of one ventricle; with it is contrasted the effect of the natural pliability of the fetal brain and the symmetrical enlargement seen in congenital cases.

Hypersecretion has been viewed as the result solely of meningitis (Gowers and others); and the effect of a nontuberculous inflammation of the choroid plexuses (and also of the walls and ependymal lining of the ventricles—Bazinsky). The possibility, suggested by Quinke, of an acute angioneurotic exudation from the choroid glands and ependyma, without fever or inflammation, as well as that advanced by Parkes Weber of extravasations in the brain cavities of fluid comparable to serous effusions into the pleural and peritoneal cavities, are mentioned.

Among the causes of obstruction to the flow of the spinal fluid from the ventricles to the subarachnoid spaces are mentioned meningitis, localized to the roof of the fourth ventricle and occluding the foramina of Magendie and Luschka (cf. Joslin's recent report of eight cases of hydrocephalus following meningitis showing this selective preference), plugging of the aqueduct of Sylvius by proliferation of neuroglia, by extension of inflammatory processes from the neighborhood, by pressure of neighboring tumors, and finally by congenital malformations. Similar causes may affect the foramina of Munroe, one or both. The inflammatory process may be tuberculous, or syphilitic, or due either to other known bacteria or to some unknown virus. Experimentally it may be produced by the injection of irritating substances (aleurinat—Thomas). In some cases no cause for the cellular proliferation is demonstrable.

Schlapp and Gere suggest that in the case of simple glia proliferation the cause may be found in a consideration of the life processes of these cells. Metabolism is nowhere more delicately expressed, they think, than in the highly complex chemical reactions of the cells of the central nervous system. In the highly specialized nerve cells the formative process is held in abeyance, but in the less specialized glia and ependymal cells, formative activity is easily awakened, and "it so happens that in many cases of hydrocephalus, stimulation of these cells by some irritating substance results in an active proliferative process which involves not only the ependyma but the subependymal tissues of the aqueduct of Sylvius." This process is shown in the obliterative gliosis found in their eight unselected cases of internal hydrocephalus. They think it not unreasonable to attribute many, if not the majority, of cases of congenital internal hydrocephalus to closure of the aqueduct of Sylvius through proliferation of the glia and ependymal tissues, or to the invasion of the fourth ventricle by tumors having their origin in the floor, the choroid plexus, or the membranous roof of the ventricle.

Leopold and Bernard⁴³ have examined the spinal fluid of ten normal children for nonprotein nitrogen, urea, uric acid, creatinin, and sugar. The children ranged in age from 1½ to 10 years.

According to Cushing, the cerebrospinal fluid is secreted by the choroid plexus. The cells of this plexus are relatively impermeable to the passage from the blood stream of drugs and such substances as bile pigments. Leopold and Bernhard conclude that they are also relatively impermeable to uric acid, another of the constituents of the blood, since in the normal spinal fluids examined there was a slightly positive reaction for uric acid in a few cases, but not in a single instance was there enough uric acid present to give a positive quantitative test.

The sugar content of the spinal fluid was very constant and varied between 0.07 and 0.1 per cent., the average content being 0.07—figures corresponding closely with those given by Schloss and Schroeder. The nonprotein nitrogen of the normal spinal fluid (21 mg. per 100 c.c.) averaged 75 per cent. of that in the blood.

Figures from forty-nine abnormal children, chorea, syphilis, epilepsy, tuberculous meningitis, infantile paralysis, nephritis and enuresis, are also presented. For these reference must be made to the original article.

Rachel L. Ash⁴⁴ reports a case of tuberculoma of the spinal cord in a 2-year-old infant. The family history was negative for tuberculosis.

43. Leopold, Jerome, Sr., and Bernhard, Adolph: Studies in the Chemistry of the Spinal Fluid of Children, *AM. JOUR. DIS. CHILD.*, 1917, **13**, 34.

44. Ash, Rachel L.: A Contribution to the Diagnosis of Spinal Cord Tumors in Childhood, *AM. JOUR. DIS. CHILD.*, 1917, **13**, 487.

The child had been continuously ill for four months and the following symptoms had appeared consecutively: enlarged cervical glands, torticollis, weakness in the right hand, weakness in right leg, intermittent fever and night sweats. On examination eight days before death there was a mass of enlarged and tender glands beneath the right sternocleidomastoid muscle and the neck was inclined to the right; there was stiffness of the neck; pressure over the lower cervical vertebra caused pain; there was no kyphosis or scoliosis. A roentgenogram showed no change in the cervical vertebrae. The von Pirquet test was strongly positive.

The right eye-slit was narrower than the left; there were alternate flushings over the right and left cheek, and profuse sweating of the upper portion of the body. The localizing spinal signs consisted in a history of pain or paresthesia in the right shoulder preceding a unilateral paralysis which began in the right upper extremity and passed to the right lower extremity, and was followed by weakness of the left shoulder girdle, and finally a complete paraplegia; spasticity in the lower extremities; seemingly almost complete absence of sensibility to pain below the second intercostal space (C V); sharply localized tenderness over the lower cervical vertebrae; and finally, a heavy albuminous deposit and yellow color in the spinal fluid (significant of pressure—Nonne). Cerebral signs pointing to an early meningitis appeared, but this seemed of minor importance.

At necropsy there was found an olive-shaped tumor mass, 2.5 by 1.2 cm. at the level of the fifth, sixth, seventh and eighth cervical segments. It was extramedullary and not attached to the spinal roots, and did not infiltrate these or the cord substance proper. On section it was grayish-white, homogeneous, and of caseous appearance; there was no evidence of liquefaction.

There were caseous mesenteric and other lymph nodes, numerous typical lymphoid tubercles in the cervical and dorsal spinal meninges, and a small tuberculoma of the cerebrum (cingulum), and evidences of general miliary tuberculosis.

The report is accompanied by a sketch of the tumor and the rather unusual features of the case are discussed: the absence of pain as a symptom, the occurrence of xanthochromia of the cerebrospinal fluid with massive coagulation, and the position of the tumor. It appears (Schlesinger) that meningeal tumors are more frequent in adults than children. In children extramedullary tumors are usually extradural lipomas or masses of tubercle; tuberculomas appear within the cord.

Curable Tuberculosis of Nervous Centers.—G. Fiore published in 1911 a case of cerebral tuberculosis which resulted in a cure; and in 1913 an article showing the condition to be anatomically curable. He

came to the conclusion that the axion of the incurability of meningeal tuberculosis could not longer be maintained in an absolute manner. He⁴⁵ now reports another case of tuberculous meningitis in which recovery was complete.

A child 8 years of age, who had had convulsions when 1 month old, pertussis at the age of 9 months, and scarlet fever at 6 years, was admitted to the hospital with marked signs of lymphatism and tracheo-bronchial adenitis; von Pirquet strongly positive. At the same time there was a bronchopneumonia which cleared up, leaving only a patch of harsh breathing at the apex of the right lung. Shortly afterward there occurred vomiting, headache, drowsiness, irregular fever, increased reflexes, persistent dermatographia and marked cranial tympany on percussion. Lumbar puncture gave abundant clear fluid under pressure, which produced tuberculosis in a guinea-pig. The patient continued in the same state for more than a month and then began to improve, regaining consciousness. The residual signs of apical bronchopneumonia disappeared. Lumbar puncture was performed eight times, the pressure diminishing *pari passu* with the amount of albumin and cells. After five or six months the recovery was complete.

Sharpe⁴⁶ describes the pathologic findings in a 3½-year-old Hebrew girl who was sent to the Willard Parker Hospital as a case of measles with purpura. The child was said to have been ill six days with measles and the rash to have disappeared after four days. On admission there was a widespread purpura with a remarkable vermilion border in the larger areas. The purpuric areas varied from small petechiae to suffusions 4 to 4½ inches in diameter. They were present on the buccal surface, conjunctivae, face, trunk and extremities. The child was apathetic, unconscious, and presented a marked tremor. There was almost complete absence of cerebrospinal involvement. Lumbar puncture yielded purulent fluid with meningococci. These were also obtained from the blood.

Microscopic examination with the Gram stain was unsatisfactory, but with the Pappenheim-Saathoff stain meningococci were demonstrated, both intracellular and extracellular within the capillaries as well as free in the tissues.

Sharpe says that according to Koplik (Osler's Modern Medicine, Ed. 1, pp. 502-513) the intracellular diplococcus has been found in subcutaneous abscesses, but not in herpes of the face and trunk, or in puru-

45. Riv. clin. pediat., 1916, 14, 181.

46. Sharpe, C. T.: Meningococcus Meningitis with Unusual Hemorrhagic Manifestations and Demonstration of the Diplococcus in the Skin, Arch. Pediat., 1916, 33, 641.

lent infiltration or abscesses of the skin. Since it has been demonstrated in the blood, it is not unexpected that it should be found in the skin in cases of cutaneous hemorrhages, as in this instance.

Koplik⁴⁷ contributes an article on meningitis in the new-born. He thinks the condition is overlooked, or at first scarcely suspected, because the newly born infant does not react to infection in a way to attract attention, and reacts very slowly to cerebral irritation. It is only after the symptoms of cerebral pressure have developed that the case is suspected of being one of meningitis. The symptoms in the new-born which should lead to such a suspicion are convulsions, repeated, with convulsive movements of the eyes and muscles of the extremities in the intervals, fever, constant restlessness, with vomiting, accompanied by a suppressed groaning respiration and a temperature curve that is at first very high, then gradually remitting, or intermitting, and falling to or near normal. Opisthotonus is slow in developing. The diagnosis most commonly ventured is tetany.

Bacteriologic examination of the spinal fluid in twelve cases showed streptococcus in four, meningococcus in four, pneumococcus in three, and colon bacillus in one.

The colon bacillus case was the result of a severe *B. coli* pyelitis. The child developed hydrocephalus and died later in infancy. One of the children with meningococcus meningitis survived, but with hydrocephalus. The other two children died.

James Warren Sever⁴⁸ of the Children's Hospital, Boston, reports an extensive study on obstetric paralysis, its etiology, pathology, clinical aspects and treatment, with a statistical study of 470 cases. He concludes that traction on the brachial plexus, with resultant injury of the plexus, is the cause of the condition. Two types are recognized, the typical upper arm type and a typical lower or whole arm type. Numerous cuts from obstetric and other manuals are reproduced to show how this traction is produced during birth and obstetric procedures. By numerous dissections on infantile cadavers the author has satisfied himself that traction and forcible separation of the head and shoulder puts the upper cords, the fifth and sixth cervical roots of the brachial plexus, under dangerous tension—tension so great that the two upper cords stand out like violin strings; and that any sudden force applied with the head bent to the side and the shoulder held would without question injure these cords. Forcible abduction and elevation of the arm and shoulder, on the other hand, a condition seen in breech cases

47. Koplik, H.: Meningitis in the New-Born and in Infants Under Three Months of Age, *Arch. Pediat.*, 1916, **33**, 481.

48. Sever, James Warren: Obstetric Paralysis: Its Etiology, Pathology, Clinical Aspects and Treatment, with a Report of Four Hundred and Seventy Cases, *Am. Jour. Dis. Child.*, 1916, **12**, 541.

with the arm extended, puts the lower cords of the plexus, the eighth cervical and first thoracic, on a stretch, and when much force is applied it may well lead to a tear, rupture, or other injury of these segments.

In the first instance, when force was applied, experimentally, the suprascapular nerve always snapped first, apparently because it had not so much freedom of play as the other nerves. In the fifth and sixth cervical nerves the experimental lesion was not a complete tear, but a fraying out of the nerve inside the sheath, followed by partial tearing or rupture of the sheath, which always gave way first. In some instances, evulsion from the spinal cord of the fifth and sixth cervical roots occurred. The subsequent developments are described. Corrective operations are discussed and advocated, and the prognosis for a useful arm is held to be good in the upper arm type and bad in the lower arm type. The paper is well illustrated.

Coplin⁴⁹ presents facts in support of a contention that there is a type of renal anomaly of developmental origin which predisposes to or renders inevitable some form of nephritis, and that this congenital abnormality is probably primarily a defective arteriogenesis occurring of necessity early in the involution of the organ. The condition of renal hypogenesis (renal agenesis, renal disparity, etc.) is recognized by systemic writers and authors of textbooks. Coplin thinks that the clinician should today be able to recognize it. Besancon (Thèse de Paris) lays particular stress on history of chlorosis or of a chlorotic appearance, headache, vomiting, lassitude, slightly puffy eyelids, slight diffuse edema of the lower extremities, frequent micturition, pale and abundant urine. Coplin adds that nephritis, toxemia, or uremia, coming on in young persons without adequate cause should arouse suspicion, and states that the condition has already been recognized by the use of modern clinical methods, and operated on.

From the nonspecific character of the symptoms enumerated, and the difficulty attending special examination in young children, it would seem unlikely that such a diagnosis could be made clinically in young children.

Young and Davis,⁵⁰ in reporting a case of (left sided) double kidney and ureter occurring in a man of 57 years, say that an average of the estimates of various observers places the frequency of ureteral duplication at about 3 per cent. of all individuals. Double ureter and double kidney constitute a much rarer anomaly. The lesions are accounted for embryologically by a premature or exaggerated bifurcation of the

49. Coplin, W. M. L.: Unilateral Renal Hypoplasia and Diplasia Due to Defective Arteriogenesis: Relation to So-Called Hypogenetic Nephritis, *Am. Jour. Med. Sc.*, 1917, **153**, 381.

50. Young, Hugh H., and Davis, Edwin G.: Double Ureter and Kidney, etc., *Jour. Urology*, 1917, **1**, 17; Abstr. in *Bull. Johns Hopkins Hosp.*, 1917, **28**.

tip of the ureteral bud, the split extending varying distances down the ureteral stalk. Normally the bifurcation takes place to a limited extent, being confined to the primitive pelvis. When the extent of this normal bifurcation or splitting is excessive, two separate pelves and a bifid ureter are produced. In such cases one may speak of a "cleft ureter" or a "double ureter," according as the ureters do or do not have separate openings into the bladder (Felix). "Complete double ureter is considered to be formed either as the result of two separate evaginations from the Wolffian duct, or as the result of the process of dilatation of the lower end of the Wolffian duct (and of the uncleft lower end of the ureter) by which the former comes to form a part of the bladder wall." As the finer methods of renal diagnosis come to be more generally applied, it is probable that examples of this anomaly will be found more frequently.

In surgical literature about twenty-six only are reported. Most of these were treated by complete nephrectomy though in a majority of them it was definitely stated that half of the excised kidney was normal. The lesion involved the upper segment in 80 per cent. of the cases.

Simon Engländer⁵¹ reports an instance of diverticulum of the urethra.

Vaglio⁵² has reported on the occurrence of hydrocele in nursing infants, as it appears in the clinic at Naples (Professor Jemma), and the relation of the condition to syphilis. He finds that in nurslings with varied manifestations of hereditary syphilis, periorchitis serosa occurs in a little more than 17 per cent. of the cases. In other cases hydrocele occurs as the only symptom of hereditary syphilis.

In fifty-five cases of hydrocele in nurslings between 0 and 1 year of age, he found syphilitic infection coexisted in twenty-four, and could not be excluded certainly in five; that is, syphilitic infection coexisted in 40 per cent. of the cases of hydrocele.

Syphilitic lesions of the testicle are recognized as most frequent in infants. According to Hart the process is a diffuse interstitial cellular proliferation, shown clinically (Henock) in increased size and non-painful induration of the part, unaccompanied by special subjective symptoms and never leading to suppuration. Coexistence of a serous periorchitis, or its development at the time of visiting the clinic, would account for the condition found by Vaglio.

Of the nonsyphilitic cases in Vaglio's series, one occurred in connection with a lesion of the skin of the scrotum and six with distur-

51. Jour. Am. Med. Assn., 1917, **68**, 351.

52. Vaglio, R.: Contributo alla etiologia dell' idrocele dei lattanti, *La Pediatria*, 1917, **25**, 212.

bances of nutrition; in the remaining nineteen no possible etiologic cause was apparent.

Lewin⁵³ offers a clinical report of two cases of acrocephaly—one a 6-year-old colored boy, the other an adult. He defines acrocephaly, or tower-head, as a syndrome consisting of a dome-shaped skull with characteristic roentgen-ray findings, exophthalmos and optic nerve changes, associated with some minor abnormalities, such as a high arched palate and deformities of the hands or feet. When combined with deformities of the hands or feet, the name acrocephalosyndactylism is applied. The condition was first definitely recognized and described by von Graefe in 1866. Nearly 100 cases are now recorded. Numerous recent references accompany the report.

Ehrenfried⁵⁴ reports twelve cases of hereditary deforming chondrodysplasia; with multiple cartilaginous exostoses and reviews American literature on the subject.

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53. Lewin, Philip: Acrocephaly, with a Report of Two Cases, *Am. Jour. Dis. Child.*, 1917, **13**, 61.

54. Ehrenfried, A.: Hereditary Deforming Chondrodysplasia; Multiple Cartilaginous Exostoses: A Review of the American Literature and Report of Twelve Cases, *Jour. Am. Med. Assn.*, 1917, **68**, 502.

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CUTANEOUS AND INTRACUTANEOUS TUBERCULIN TESTS IN INFANTS AND CHILDREN *

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NEW YORK

With the introduction of simple and harmless methods for the determination of the presence or absence of tuberculous infection, our knowledge of the prevalence of tuberculosis has made immense strides. The work of von Pirquet, Schick, Hamburger, Ghon and many others has taught us that tuberculous infection is common, much more common than we had previously believed; that its incidence in childhood increases as the age of the child advances; that tuberculous infection is by no means synonymous with tuberculous disease. Moreover, we are now in possession of much evidence which proves (1) that the respiratory tract is in a very large percentage of cases the portal of entry; (2) that the bronchial lymph nodes are the seat of tubercles in almost all children who react positively to tuberculin tests; and (3) that the great majority of cases of adult pulmonary tuberculosis probably depend on these very nodes for their source of origin.

In spite of all this advance in our knowledge, however, there is still a great deal to be learned about the tuberculin reaction as it affects children.¹ We were led to collect some data on this subject by the following occurrence: In our institution, a large asylum for infants and young children, it was customary to perform von Pirquet tests on all the children admitted. Wishing to obtain some information concerning the reaction, we chose a number of children who had reacted positively six months previously, and retested them. To our surprise, quite a number of them failed to react. In many of these children the test was repeated several times in the course of a few days, and the reaction then changed from negative to positive.

This occurrence showed quite definitely that the reactivity of the individual undergoes change, and that although a single positive reaction means the presence of tubercle, the power of response to tuberculin may be so altered by time that the same individual, though undoubtedly still the subject of tuberculous infection, fails to respond to the same tuberculin dose. For all clinical purposes, a single or at

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* From the Home for Hebrew Infants.

1. An excellent compilation of the literature on this subject may be found in "La Tuberculose de l'Enfant" by L. Jeanneret, Paris, 1915.

most two tests may be sufficient, but when we are attempting to gather statistics as to the frequency of tubercle infection, this is by no means sufficient. In a search of the literature we could find only very few records where systematic attempts had been made, in a large group of children, to push to its limit the possibility of obtaining a positive reaction. We therefore set ourselves the task of repeatedly testing a large number of infants and young children in the hope of uncovering, as it were, many hidden cases of latent tuberculous infection.

Of the various local tuberculin tests devised, the most commonly employed in children have been (1) the von Pirquet test, the cutaneous application of tuberculin through an abrasion in the skin; (2) the *Stichreaction* of Escherich, local redness at the site of a subcutaneous injection of tuberculin; (3) the conjunctival reaction of Wolff-Eisner and Calmette; (4) the cutaneous reaction of Moro, the reaction to tuberculin rubbed into the unabraded skin; (5) the intracutaneous test of Mantoux.

Of these the Moro test and the conjunctival reaction have been generally abandoned. The von Pirquet test, owing to its simplicity, has found the greatest favor, and has been very extensively employed. The *Stichreaction* has been studied by Hamburger, who was able to show that it was much more delicate than the von Pirquet test. The method had been described many years ago by Escherich and Ebstein, but neither had thought it of a specific nature, and it was only after the specificity of the cutaneous test had been shown by von Pirquet and Schick that attention was again drawn to the *Stichreaction*. The positive reaction is described as an area from 18 to 30 mm. wide at the site of the subcutaneous injection, red in color, sometimes raised and often painful. It usually appears from eighteen to twenty-four hours after the injection, increases during the second day, diminishes on the third, and after four or five days leaves a brownish discoloration. Very small amounts of tuberculin are sufficient to give a positive reaction, 0.001 mg. being sufficient. The great advantage of the *Stichreaction* over the cutaneous are twofold: first, it is much more delicate; second, we know the exact dosage and concentration of the tuberculin used, and can therefore, as it were, titrate the patient's susceptibility. Cases which react to 0.001 mg. or more intradermally, usually also react positively to the cutaneous test. On the other hand, those persons with an intradermal test positive to smaller amounts of tuberculin, usually fail to show a positive von Pirquet reaction. According to Hamburger, the majority of active cases have a susceptibility to at least 0.001 mg. Inactive tuberculosis, on the other hand, reacts positively to the cutaneous test in only two thirds to three quarters of the cases.

A modification of this test, for which even greater delicacy is claimed, was introduced by Mantoux and Roux in 1909. Instead of the subcutaneous, they employed the intracutaneous route. They used a 1:5,000 solution of tuberculin in normal salt solution and injected one drop, that is, 0.01 mg., of tuberculin directly into the skin by means

of a very fine needle. They claimed that the positive reaction was well marked, appearing as an infiltration surrounded by a red areola, the reaction attaining its maximum at forty-eight hours.

Subsequent investigators have modified the dosage in this test, some using graduated amounts of tuberculin, thus obtaining information not only as to the absolute presence or absence of tuberculous infection, but also as to the titer of the patient's ability to react.

Since so many reports were encountered in which conclusions were drawn from a single von Pirquet test, and since it seemed definitely proved that the intradermic test was the most delicate, we decided on the following procedure: Each child was given a von Pirquet test which was observed after twenty-four, and again after forty-eight hours. If positive, this was regarded as evidence of tuberculous infection. If negative after forty-eight hours, a second von Pirquet test was performed. After forty-eight hours a third test was made. If this proved negative, an intradermic injection of 0.1 c.c. of 1:1,000 old Koch tuberculin (that is, 0.1 mg.) in saline solution was given. If after forty-eight hours this was negative, 0.1 c.c. of a 1:100 solution (that is, 1 mg.) was injected and repeated after forty-eight hours if negative. If after these six tests the case still failed to react, it was considered definitely negative. In all, 1,165 tests were made on 206 children.²

The children tested were inmates of an infant asylum in which the hygienic conditions are of the best. None of the infants or children at the time of testing showed any clinical manifestations of tuberculosis, nor were any of them tested during the course of an acute illness. The children varied in age from a few days up to 6 years. They were drawn from the poorest class of New York City's Hebrew population.

Table 1 will give a general view of our results. In all, fifty-two children showed a positive reaction to some of the tests, giving a percentage of 25.2; that is to say, one quarter of the population of the asylum had been at some time infected with the tubercle bacillus.

2. The von Pirquet tests were made with undiluted old tuberculin, obtained from the New York City Board of Health Laboratory, a regular von Pirquet scarifier being used. For the intradermic tests an all glass hypodermic syringe and fine needle were used. Care was taken that the needle was thrust into and not under the skin, this being ascertained by the appearance of a tiny wheal as the solution was being forced between the layers of the skin. All tests were made on the flexor surface of the forearm, after cleansing with alcohol, and were read after a period of forty-eight hours, since it is generally conceded that any traumatic action has by that time disappeared.

As these tests were carried out over a period of two years, it was obviously impossible to make use of the same solution of tuberculin for them all. Many of them, however, were done with the same solution, and in no child was different tuberculin used for the different tests; that is to say, the three von Pirquet and the three intradermic tests were always performed with the same stock tuberculin.

TABLE 1.—REACTION TO MULTIPLE CUTANEOUS AND INTRACUTANEOUS TUBERCULIN TESTS (206 CHILDREN), 52 POSITIVE REACTIONS

Age	First Test (v. Pir- quet) Posi- tive	Second Test (v. Pir- quet) Posi- tive	Third Test (v. Pir- quet) Posi- tive	Fourth Test Intra- cuta- neous 0.1 Mg. Posi- tive	Fifth Test Intra- cuta- neous 1 Mg. Posi- tive	Sixth Test Intra- cuta- neous 1 Mg. Posi- tive	Total Posi- tive	Total Neg- ative
0-6 mos.	2	0	0	0	2	0	4	47
6-12 mos.	2	0	1	0	2	1	6	32
1-2 yrs.	0	1	1	1	2	0	5	24
2-3 yrs.	1	3	0	2	5	3	14	31
3-4 yrs.	0	1	3	1	1	0	6	7
4-5 yrs.	1	1	1	2	1	0	6	10
5-6 yrs.	1	1	1	7	0	1	11	8

TABLE 2.—RESULTS OF CUTANEOUS AND INTRACUTANEOUS TUBERCULIN TESTS ON 206 CHILDREN, SHOWING THE INCREASED NUMBER OF POSITIVE REACTIONS AS THE TESTS ARE REPEATED

	Number of Positive Cases	Peren- tage
One cutaneous test.....	7	3.3
Two cutaneous tests.....	14	6.8
Three cutaneous tests.....	21	10.1
Three cutaneous and one intracutaneous tests (0.1 mg.).....	34	16.5
Three cutaneous and two intracutaneous tests (0.1 mg.; 1 mg.).....	47	22.8
Three cutaneous and three intracutaneous tests (0.1 mg.; 1 mg.; 1 mg.).....	52	25.2

Table 2 has been compiled to show the great importance of retesting the negative cases. It will be seen that if we had employed but a single von Pirquet test we should have drawn the incorrect conclusion that only 3.3 per cent. of the inmates had been infected with the tubercle bacillus. If we had used two von Pirquet tests and stopped there, the percentage would have been doubled (6.8), and so on, until by the use of the intradermic tests the true percentage of infected cases was found to be 25.2.

In Table 3 we have arranged the cases according to their ages and have calculated the percentage of positives in each age group. It is very interesting to note the step-like increase in the disease incidence with increasing age. Thus out of fifty-one cases under 6 months of age, four reacted positively, a percentage of 7.8. Of children in the second six months 15.8 per cent. were positive; of those from 1 to 2

years old, 17.2 per cent. were positive; of those aged from 2 to 3 years, 31.3 per cent. were positive; of those aged from 3 to 5 years, 42.8 per cent. were positive; and finally of the children aged from 5 to 6 years, 78 per cent. were positive.

A consideration of these results leads to some interesting deductions. An important fact to be emphasized is that any series of examinations designed to ascertain the incidence of tubercle infection must consist of more than a single test in each individual case. In the case of the intradermal application of tuberculin in milligram doses, the change from a negative to a positive reaction may be supposed to be due to the sensitizing influence of the previous dose. In the case of the von Pirquet test, however, authorities seem to agree that not enough tuberculin enters the organism to change its allergy. Why a second or a third test should be positive when the previous ones were negative remains unexplained.

TABLE 3.—AGE DISTRIBUTION OF PATIENTS REACTING POSITIVELY TO CUTANEOUS OR INTRACUTANEOUS TEST

Age	Number Tested	Number Reacting Positively	Percentage
0-6 mos.	51	4	7.8
6-12 mos.	38	6	15.8
1-2 yrs.	29	5	17.2
2-3 yrs.	45	14	31.1
3-5 yrs.	28	12	42.8
5-6 yrs.	14	11	78.0

The second fact worthy of note is the great frequency with which we have encountered positive reactions. In most of the American statistics the incidence of the disease in young infants is not nearly so great as we have encountered it, and for this reason objection might be raised to our method or to our interpretation of the reactions. Several factors, however, go to show that we are dealing with true reactions and that our reading of the tests are correct. In the first place, the gradual increase in the percentage of positive cases with increased age of the children cannot be mere coincidence. In Table 3, if we look at the percentage column, we see a steady rise from the percentage of incidence in infants under 6 months, to children in their fifth year of life. (We have grouped together the children in their third to fourth year and those in their fourth to fifth years, since we have had so few at each of these ages.) As is well known, the tuberculin sensitiveness does not become manifest before the tenth week of life (Loewenstein), those weeks being the latent period during which the child forms the antibodies necessary for the reaction. As more and more infections

take place owing to a longer period of exposure, it is quite natural that with increased age, the number of positive reactions should grow larger.

The objection might also be raised that we had confused pseudo reactions with positive reactions. To guard against this, several experiments were performed. First, to make sure of the fact that we were dealing with a specific tuberculin reaction and not some nonspecific skin manifestation, we proceeded as follows: In twenty children, some of whom had reacted positively and others negatively, there was injected intradermally, as control, a solution of broth, peptone and glycerin, prepared in the same manner as in the old Koch tuberculin, omitting, however, the addition of tubercle bacilli. This solution, which was kindly prepared for us by Dr. H. Miller of the bacteriological laboratory of the College of Physicians and Surgeons, was diluted in the same manner as the tuberculin; that is, 1:1,000 and 1:100, and of this 0.1 c.c. was injected intracutaneously. In not a single instance was

TABLE 4.—RESULTS OF INTRACUTANEOUS INJECTIONS AND REINJECTIONS WITH THE SAME DOSE

Case	Date of First Positive Reaction	Result of Test (Size of Areola in Mm.)	Date of Retest	Result of Retest (Size of Areola in Mm.)
H. T.	May 9	Positive (7×7)	June 8	Positive (7×7)
A. H.	March 2	Positive (7×7)	June 8	Positive (25×25)
H. V.	May 2	Positive (10×10)	June 8	Positive (7×7)
G. U.	May 2	Positive (4×4)	June 8	Positive (20×20)

any reaction noted, either in children who had reacted positively or those who had reacted negatively to tuberculin. This result, we believe, definitely disposes of any objection that might be raised on the ground that we are dealing in some of our cases with a nonspecific reaction.

Further, to prove the correctness of the readings, a number of our positive cases were retested some time after the last positive reactions had been obtained, as will be seen in Tables 4 and 5. In Table 4 are tabulated four cases in which 0.1 mg. tuberculin had caused definite but small sized reactions. On account of the relatively small reactions, these children were retested from one to three months later with a single intracutaneous dose of 0.1 mg. All four patients gave definite, positive reactions.

In Table 5 are shown the records of seven cases chosen at random among that group which had failed to react to the three von Pirquet tests and also to the intracutaneous test with 0.1 mg., the reaction only appearing when 1 mg. was used. Thinking that these children's

reactivity might have been altered with time and with the previous administration of tuberculin, we reinjected them at a period of from two to three months later, with 0.1 mg., a dose to which all of them had previously failed to react. As will be seen in the table, all but one patient showed definite marked positive reactions. This one child, Mary G., was then reinjected forty-eight hours later with 1 mg., to which she reacted with positive reaction similar to the one she had shown two and one half months previously.

We have, therefore, eleven cases which were retested and of these every patient without exception continued to react with a positive reaction.

As a matter of interest, an attempt was made to repeat the 1 mg. intradermal tests on infants who had reacted negatively to the six routine tests. These infants, four in number, were reinjected with

TABLE 5.—RESULTS OF INTRACUTANEOUS INJECTIONS AND SUBSEQUENT REINJECTIONS WITH SMALLER DOSE

Case	Date of Negative Reaction (0.1 Mg.)	Date of Positive Reaction (1 Mg.)	Date of Reinjection (0.1 Mg.)	Result of Reinjection (Diameter of Areola in Mm.)	Remarks
P. S.	April 27	April 30	June 8	Positive (12×12)	
I. B.	April 27	April 30	June 8	Positive (30×30)	
S. S.	April 15	April 18	June 8	Positive (10×12)	
C. S.	April 15	April 18	June 8	Positive (10×10)	
M. G.	March 25	March 28	June 8	0	Retested again June 10 with 1 mg.; positive reaction (12×12)
H. B.	March 25	March 28	June 8	Positive (7×7)	
L. H.	March 25	March 28	June 8	Positive (10×10)	

1 mg. every other day for two weeks (seven additional tests), but all of them remained consistently negative.

When we compare our results with those of other investigators we find that our results are in accord with a number of those who have used the intracutaneous method. Many other series, however, especially those in which the von Pirquet test alone was relied on, show much lower percentage of positive reactions. Table 6 shows the results obtained by investigators who have used the von Pirquet and the intracutaneous tests.

The most recently published large series of American cases is that of Veeder and Johnston.³ Our results and theirs do not agree, though it is perhaps not fair to compare them, since these authors themselves state that their "figures do not represent a special study of the fre-

3. Veeder, B. S., and Johnston, M. R.: AM. JOUR. DIS. CHILD., 1915, 9, 478.

quency of tuberculin reactions in childhood, but the results of tests made for diagnostic purposes on hospital patients regardless of the cause for their admission." As our figures do represent a specially intensive search for positive reactions, it is natural that they should be higher. Then, too, as many authors, including Veeder and Johnston, have pointed out, the environment and social status of the particular group of children investigated must make a vast difference in the figures obtained. In one particular, however, we must absolutely disagree with the last named authors, and that is on the question of the greater delicacy of the intradermic tests as compared with the von Pirquet. Veeder and Johnston say, "The intradermic tuberculin test

TABLE 6.—FREQUENCY OF POSITIVE TUBERCULIN SKIN REACTIONS IN CHILDHOOD ACCORDING TO VARIOUS INVESTIGATORS *

I. Oalmette, Grysez and Letulle (1,226 children examined)		Méros and Khalatoff (Geneva)		Mantoux and Lemaire (800 children examined)	
	Per Cent. Positive		Per Cent. Positive		Per Cent. Positive
0-1 yr.	8.7	0-6 mos.	0.0	1-2 yrs.	16.0
1-2 yrs.	22.1	6-12 mos.	6.6	2-4 yrs.	51.0
2-5 yrs.	53.8	1-2 yrs.	17.6	4-7 yrs.	66.0
5-15 yrs.	81.4	2-3 yrs.	40.0	7-15 yrs.	82.0
		3-5 yrs.	51.0		
		5-7 yrs.	61.2		
		7-10 yrs.	66.4		
		10-15 yrs.	78.7		
II. Karl Kaspar (Erlangen)		Apteckmant (Paris)		Mantoux (174 children examined)	
0-1 yr.	10.0	0-1 yrs.	0.5	0-1 yr.	2.5
1-2 yrs.	31.7	1-2 yrs.	16.0	1-3 yrs.	29.0
2-4 yrs.	30.0	2-5 yrs.	48.0	3-7 yrs.	50.0
4-14 yrs.	60.0	6-10 yrs.	68.0	7-15 yrs.	80.0
		11-15 yrs.	78.0		
				Morgenroth	
				200 infants.....	5.0

* Quoted from L. Jeanneret: *Rev. méd. de la Suisse romande*, 1913, **33**, 371.

has given but a slight increase in the percentage of positive reactions over the percentage of positive cutaneous reactions." In our method of procedure, however, we found only twenty-one positive reactions when the von Pirquet test alone was employed, whereas of the remaining 185 children, thirty-one reacted to the intracutaneous test.

In all probability, if the intracutaneous method had been used alone, to the exclusion of the von Pirquet test, the results would have been identical as far as concerns the discovery of latent tuberculous infection; but we chose to use both the cutaneous and the intracutaneous application in order to compare the two, and also to show that even if one confines oneself to the von Pirquet method, the tests, if negative, ought to be repeatedly performed.

In the course of this work the fact became evident that certain of the children showed very marked local reactions, though their general condition appeared to be excellent and no clinical signs of disease could be elicited. As many of these children belonged to the "exudative diathesis" group, it seemed possible that since they were so prone to skin

eruptions, their specially violent reaction to tuberculin might be correlated with a particularly susceptible skin.

To help clear up this question a number of the children who had shown the most pronounced tuberculin reactions were subjected to different skin irritants.⁴ Mustard paste, ointments containing various percentages of cantharides and solutions of various strengths of phenol were applied to the unbroken skin for a definite period of time. Comparisons were then made between the resulting erythema of the skin with that caused by the same irritants in children who had failed to react to the von Pirquet test. All of these attempts to prove any particular skin sensitiveness in the former group of children resulted negatively. We refrain from publishing these experiments in detail since they uniformly failed to explain any cause for the very large size of some of the reactions.

Much work has been done on this particular phase of the reaction; the marked reaction has been explained as the result, on the one hand, of a severe infection, or, on the other, as a sign of marked resistance. That there is, however, a local dermal factor besides the general reactivity of the patient tested, is shown by the following experiment performed by von Pirquet:⁵

In children who had temporarily lost the reaction to tuberculin on account of an attack of measles, a cutaneous test was performed daily on different parts of the body. The reaction on the dorsum of the foot seemed larger than those on the arms, whereas the skin of the neck gave the smallest reactions. Frehn,⁶ on the contrary, found the skin of the chest most sensitive.

A critical survey of the literature, moreover, fails to show any unanimity in opinions on the subject. Von Pirquet⁷ himself says:

The cutaneous tuberculin reaction depends on at least two factors. One of these factors is the tuberculin, and the other, furnished by the organism, can be considered as an antibody, whose origin dates back to a previous infection of the organism with tubercle bacilli. . . . In persons who give the reaction, a marked difference exists between different areas of skin. In skin areas which have been subjected previously to one or repeated applications of tuberculin, the reaction proceeds in a different manner. The most prominent influence of the concentration of the antibody seems to lie in the time in which the reaction appears and reaches its maximum, whereas the absolute height of the curve, signifying the intensity of the reaction, seems to be dependent on the strength of the tuberculin.

4. Similar experiments have been reported by Holmgren, I.: *Beitr. zur Klin. d. Tuberk.*, 1912, No. 25; Rachmilewitsch: *Jahrb. f. Kinderh.*, 1913, No. 77; Entz: *Wien. klin. Wchnschr.*, 1908, No. 12, and others.

5. Von Pirquet: *Wien. med. Wchnschr.*, 1913, **39**, 2518.

6. Frehn: *Beitr. z. Klin. d. Tuberk.*, 1914, No. 32.

7. Von Pirquet: *Jour. Pharm. and Exper. Therap.*, 1909-1910, **1**, 174.

A survey of our experiments here reported reveals that infection by the tubercle bacillus is probably as frequent in America as elsewhere, and that to detect the infected children, frequently repeated tests are necessary. The interesting question arises as to the significance of these great numbers of latent cases. Are the children whose susceptibility is so slight that they react only to the intradermal test to be regarded as better, or less well protected against the disease tuberculosis? Is mild susceptibility synonymous with marked resistance, or only with slight infection? At present these questions cannot be answered and their solution can only be arrived at if series of individuals can be followed for longer periods of time. We are now in possession of knowledge which makes us fairly certain that the tuberculous infection acquired in childhood has a distinct bearing on the disease as it appears in later life, and it will be by following up series of cases such as are here reported, that we may arrive at some definite relationship between tuberculin susceptibility and tuberculous disease.

We wish to express our indebtedness to Dr. Alfred Hess for permission to carry on this work and for much helpful advice; also to Dr. Barenberg, Resident Physician at the Home, without whose assistance and cooperation much of this work would have been impossible.

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THE HYPERTONIC INFANT, THE CURATIVE ACTION OF ATROPIN ON CERTAIN OF ITS MANIFESTATIONS *

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The Hypertonic Infant is a definite clinical entity. It is characterized by hypertonicity of all the skeletal muscles, as shown by the ability to raise the head and grasp objects even in the early days of life, and by general spasticity. The hollow viscera show increased activity of their smooth muscle fibers. This expresses itself in the form of spasm involving practically every part of the digestive tube, and, depending on the region, presents the symptom of colic, visible peristalsis, vomiting, constipation, or any combination of these. Accompanying these symptoms is marked psychic irritability, expressed by insomnia, general restlessness and crying. The hypertonic infant belongs to the *spasmophilic group* and presents the symptoms of *Vagotonia*.¹

Its recognition is of importance in this, that while presenting symptoms in the main of disturbances of nutrition, food regulation alone does not correct the fault, whereas treatment by the drug *atropin* is followed by rapid subsidence of symptoms, the results being so prompt and regular as to constitute specific action. The tolerance for milk which is usually low in these infants is at once materially increased, so that a normal amount may be utilized—a condition quite opposed to that existing before the atropin was begun.

In the teaching of infant feeding stress has been laid on two factors: the *food* and the *infant*. The food has been studied from many angles, with the result that there is available an ample and satisfactory variety adaptable to most cases.

The infant, too, has been studied from many angles; but few serious attempts have been made to study the possibility of altering the infant's reaction toward food, when it is found impossible to adapt the food to it, despite the fact that idiosyncrasies have been noted and differentiated. Personal experience during the last few years has convinced me that in this direction lies a field which is full of promise in that ever diminishing group of difficult feeding cases. This paper deals with only one phase of the problem and will confine itself to the

* Submitted for publication March 4, 1918.

1. Eppinger and Hess: *Vagotonia*, Nervous and Mental Diseases, Monograph 20. Ed. 2, Nervous and Mental Disease Pub. Co., New York.

consideration of one group whose adaptation to food would seem to have been accomplished through the adjustment of the vegetative nervous system.

To make clear the course of reasoning which has led to this conclusion, it is necessary to review very briefly a few points regarding the vegetative nervous system and its action.

The nervous system is made up of the sensori motor and the vegetative systems. The latter, with which only we are concerned, is subdivided into the sympathetic and autonomic. The sympathetic reacts to small amounts of epinephrin. The autonomic is all that portion not included in the sympathetic, includes the vagus, and reacts to very small amounts of acetylcholen.² Under normal conditions these systems (the sympathetic and the autonomic) are in equilibrium, producing a "tonic innervation" of smooth muscles. Stimulation of one or the other system by hormones or other factors may produce contraction and spasm or paralysis.

Vagal stimulation, for instance, may cause turbulent gastric peristalsis which readily changes into retrograde peristalsis and may manifest itself in vomiting. Hence the benefit on cardiospasm and pylorospasm of atropin. If the motor vagus endings in the intestine are stimulated by pilocarpin or physostygmim, peristalsis is increased, and emptying of the bowel occurs. Under certain conditions, however, a tonic spasm of the sphincters may result, a hypertonicity with a spastic condition of the intestinal tract.¹ The opposite effect, a relaxation and quieting of the intestines follows the use of atropin, which paralyzes the vagus. Owing to its close relation to the glands of internal secretion, the autonomic nervous system doubtless has a marked influence, not only on the pancreas and the thyroid gland, but also on the entire mechanism of metabolism.¹

In the present imperfect state of our knowledge regarding the effects of food on the infant organism, it is not strange that a certain number of infants react in an abnormal way to the food introduced into the body. A normal healthy infant fed on the breast takes its food at intervals with apparent satisfaction, does not vomit, has normal stools, and sleeps most of the time between feedings, grows in size and increases in weight regularly. A normal, healthy infant fed artificially usually reacts in a similar manner.

A number of apparently normal, healthy infants fed on the breast, take their food with seeming satisfaction, grow and increase in weight, but are unhappy and restless, cry more or less constantly, sleep only at intervals for short periods of time, vomit and are constipated.

2. W. H. Gaskell: *The Involuntary Nervous System*, Monographs on Physiology, Edited by E. H. Starling.

A much larger number of artificially fed than breast fed children react in this abnormal way and present this picture of unhappy, restless, sleepless, crying infancy. The cause of this state is to be sought in the manner in which the individual child reacts to its food. Where the fault lies is not readily discernible. Available laboratory methods by which the offending substance or combination of substances can be detected and removed from the diet are lacking. The correction by the usual clinical methods of experimentation with various foods, and their combinations, is a very slow one and one not always followed by success. It is to this group of cases, whether breast or artificially fed, that the present paper desires to call attention. The cases are fairly common, and extremely intractable unless treated in the manner to be referred to.

In this group are to be found: (a) the colicky baby; (b) the sleepless baby; (c) the restless baby; (d) the irritable baby which does not prosper on any food, although there is neither gastric nor intestinal indigestion; (e) the baby suffering from pylorospasm accompanied by vomiting, usually projectile in type; (f) the constipated baby.

Without exception these infants are of the spasmophilic diathesis; and usually with a neurotic ancestry.

That usual therapeutic procedures and rearrangement of diet are inadequate to relieve the symptoms is amply demonstrated by the fact that these cases drift from physician to physician to be relieved finally by time; that is, when the age is attained when solid food is used, or by operation when pyloric obstruction is diagnosed.

The typical history is about as follows: Infant born at full term, entirely normal, fed at the breast, cries more than it should during the early days of life and is supposed to be having a great deal of colic. Beginning at once, or after several weeks, vomiting ensues; this is usually explosive but need not be of this type. The vomiting is not related to the taking of food and may occur after each nursing period, or only once or twice in twenty-four hours. The volume may be more than has been taken in at one nursing. Its very irregularity is characteristic. Because of this vomiting and irritability, changes are made in the diet, first, by modifying the breast feeding, in time, in quantity and by dilution. Usually this is ineffective. Artificial feeding is then begun and the condition becomes worse instead of better. The infant may gain normally, make only meager gains, or fail to gain at all. The infant is constipated, sleepless, and cries much more than it should.

These cases pass from hand to hand, changes are made in formula and method, but usually without much result. The diagnosis, where propulsive vomiting exists, is pylorospasm. And this is the correct diagnosis. Wherever the propulsive vomiting does not exist, the diagnosis is not made.

SYMPTOMATOLOGY

The symptomatology depends on when these children are first seen. Their weight is normal in the beginning; after some months they are

below normal and frequently rachitic. The infants without exception are hypertonic. They are able to raise their heads at birth, and grasp objects firmly. They can support themselves on their legs at the end of six or eight weeks if held up. The entire body may be raised by the head because of the rigidity. They are often referred to by the nurse and family as being very strong. An abdominal examination often reveals active gastric or intestinal peristalsis. One obtains the impression that they are unusually alert, they cry more or less constantly, rarely sleep except in short stretches, and are not happy babies. If this condition has not been corrected before five or six months, the emaciation may be marked.

Cases of this type present, in the order of their importance:

1. *Vomiting*, which, as before mentioned, is characteristically irregular, often with visible peristalsis.
2. *Crying*, which is more or less constant and violent.
3. *Insomnia*; this is usually a striking symptom, and with the crying creates a household state bordering on demoralization.
4. *Constipation*, resistant to ordinary laxative and dietetic treatment, and distinctly spastic in type, the stool being soft after it has once started.
5. *Cold Extremities*, with pallor, cyanosis and subnormal temperature. This is met with only occasionally.
6. *Underweight*; the degree depending on the age at which correct treatment is instituted—under 8 weeks, 1 to 1½ pounds; from 3 to 6 months, 3 to 4 pounds.

TREATMENT

Correct therapy shows results in this condition which are unusual in their regularity and in the rapidity with which they occur. Where indigestion exists, this of course must be improved by appropriate methods of feeding; as a rule, however, there is no indigestion and no change in diet is necessary.

By the administration of atropin in sufficient doses the entire picture changes in from forty-eight to seventy-two hours; in some cases even in twenty-four hours. The method of administering the atropin is in 1:1,000 solution, beginning with 1 drop in each bottle of food and increasing it in forty-eight hours, if there is no improvement, to 2 drops in each bottle, and later to three or four or more drops, if necessary, with an interval of forty-eight hours between change in dosage.

If the diagnosis is correct, it will be found that the atropin controls the frequency of the vomiting. The child begins to sleep very much better and for longer periods; in its waking moments it is comfortable, and cries less or not at all. The vomiting usually ceases entirely or only occurs at rare intervals. Occasionally, one symptom of those enumerated persists long after the infant is in all other respects normal, and that is usually found to be due to some faulty detail in manage-

ment. As a rule 1 or 2 drops of atropin at each feeding are enough, although frequently 3 or 4 drops or more are necessary to obtain a result. At intervals the atropin is reduced in amount, then discontinued. If there is no recurrence of symptoms, it is no longer required; if, however, the symptoms return, then the atropin must be resumed until repeated testing has shown it to be no longer necessary. This may require months; in some cases six months.

There have been no ill effects noticed from these large doses of atropin in infants, and it is a striking fact that infants a few months of age are able to take doses of atropin which would cause toxic symptoms in the adult.

If atropin is used early and in sufficient dosage the number of cases of pylorospasm which finally reach the operating table as cases of hypertrophic stenosis will be reduced to an unimportant minimum.

It is not to be supposed that all infants who vomit, or cry, or do not sleep, or are constipated will respond to this treatment. On the contrary, if the cause is elsewhere than in the autonomic nervous system, there will be no result.

DIAGNOSIS

How is it possible to make a positive diagnosis? It is not possible to make a positive diagnosis by clinical methods, but one can make a probable diagnosis when the combination of vomiting, insomnia, crying, constipation and, sometimes, subnormal temperature exists in the presence of hypertonicity and in the absence of faulty feeding. Atropin, administered in full dose, will definitely establish the diagnosis.

The maximum dose of atropin used in twenty-four hours was 1/15 grain. The maximum amount administered in a single dose was 1/16 grain, where a mother at the Welfare Station at Lebanon Hospital misunderstood directions and gave a teaspoonful of a 1:1,000 solution instead of 1 drop, to a baby under 6 months. There were no ill effects.

The earliest symptom of the physiologic effects of atropin in infants is a flushing which gives them the appearance of having fever, which sometimes actually exists, but is usually not high, dilatation of the pupils and slight puffiness of the lids.

In two institutional infants not belonging to this group, atropin in doses of 1 or 2 drops of 1:1,000 solution, after several doses produced hyperpyrexia, abdominal distention, flushing, restlessness, vomiting and diarrhea. This syndrome could be reproduced at will. Atropin in small doses paralyzes the efferent nerve endings which terminate in peripheral ganglia (for example, vagus) and in involuntary muscle. Atropin in large doses paralyzes the secretory fibers of probably all glands, including mucous glands, pancreas and liver; stops the movements and paralyzes the involuntary muscular fibers of the intestines so that they only contract feebly or not at all when directly irritated.³

3. Brunton: *Pharmacology, Therapeutics and Materia Medica*. Ed. 3, Lea Bros., Phila.

Atropin by virtue of the greater than normal transmission of blood through the tissues increases metabolism and results in an increased elimination of waste products.⁴

Perhaps the description by a nurse in charge of one of these infants (Case 1), written at my request, will give a better picture than could be obtained in any other way.

REPORT OF CASES

CASE 1.—Referred by Dr. George L. Brodhead. Edward R., born March 8, 1917; normal delivery; mother of nervous, apprehensive type; baby weighed 7 pounds 8 ounces. Breast feeding was started on the fourth day. The baby

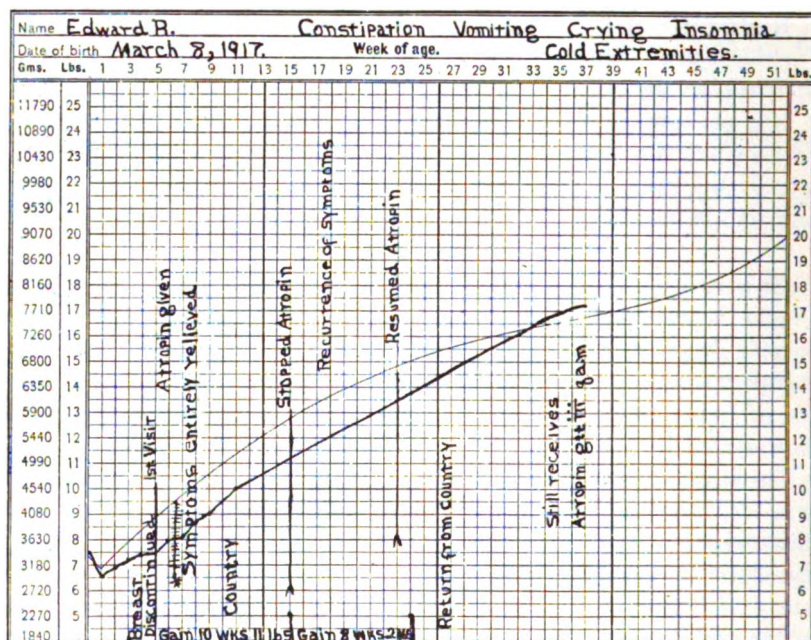


Chart 1 (Case 1).—Weight chart of Edward R.

obtained 1½ ounces on the fifth day every three hours. Meconium stools for three days. Castor oil, minims 10, produced a large mucous stool. The baby vomited mucus frequently for the first two and a half days. Lost 1.6 pounds by end of the first week. Temperature always between 98 and 98.2 F.

Second Week: The infant cried one to two hours in twenty-four; obtained on an average 2 ounces at each nursing; stools normal; gained 6 ounces. Weight 6 pounds 14 ounces.

Third Week: Cried two to two and a half hours in twenty-four; received 2½ ounces at each nursing; stool normal; three to four daily passed with a large amount of flatus and considerable distress. Gain, 5 ounces. Weight 7 pounds 3 ounces. Mother up part of the day now; very nervous and depressed (condition not caused by baby).

4. Bartholow: *Materia Medica and Therapeutics*. Ed. 11, Appleton and Co., New York.

Fourth Week: Baby cried as though in pain three to four hours daily. (a) Given barley water, $\frac{1}{2}$ ounce before each three-hour nursing; (b) given two feedings of 5-20 whole milk, with 1 ounce lactose in twenty-four hours. Regurgitated about $\frac{1}{2}$ ounce after three feedings daily. Vomited 1 to 4 ounces of sour curds after two feedings. Vomiting and regurgitation always occurred at time of stools and crying periods, which varied from day to day, most frequently occurring during the early morning or late afternoon. Weight increased 3 ounces. Weight 7 pounds 6 ounces.

Fifth Week: Breast nursing discontinued. (c) Baby given 3 ounces 6-20 whole milk; regurgitated 1 ounce of each feeding; cries six hours daily, frequently holding breath; colic (?); no relief obtained by gastric lavage, which showed a clean, sweet stomach two hours after feeding, or colonic irrigations, which were almost impossible to give as the anus became tense and contracted, then relaxing; no stool for twenty-four hours after starting bottle feedings.

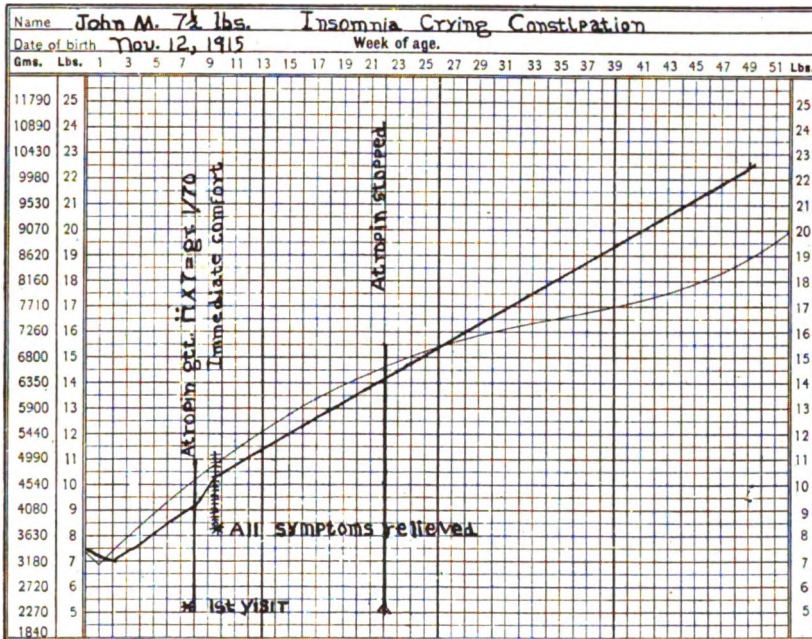


Chart 2 (Case 2).—Weight chart of John M.

Milk of magnesia, $\frac{1}{2}$ dram daily, produced one to two large, digested stools. Feedings reduced to $2\frac{1}{2}$ and then to 2 ounces; lime water in each feeding, with no change in amount or frequency of vomiting or regurgitation. Gained 1 ounce. Weight 7 pounds 7 ounces.

Sixth Week: (First visit.) (d) Milk increased to 14 in 28 ounces; 3 ounces every two and a half hours; regurgitation and vomiting not increased by more frequent or larger feedings; crying periods the same; finger tips and lips sometimes blue after hard cry; hands clinched constantly; body tense.

(e) Dextro-maltose substituted for lactose; no improvement.

(f) Same formula continued with 1 minim atropin sulphate 1:1,000 in each two and a half hour feeding. After the third feeding a marked change was noticed in the baby's condition; first feeding retained; second and third retained for two hours; the baby then vomited about $\frac{1}{2}$ ounce of curds. It then passed a large normal stool; no laxative given. All feedings were retained on the

following day; the baby practically stopped crying; entire body comfortably relaxed; gained 3 ounces in weight.

Thirty-two hours after the first dose the baby's body felt hot; temperature 100.4 F.; face flushed, pulse 124. Atropin was omitted in the next feeding. Some puffiness under the eyes was noticed in the morning; temperature normal. Atropin 1:2,000, one-half drop, given during the day in each feeding, with some slight return of spasmodic crying and tension of body; atropin, 1:1,000 given in two succeeding feedings; condition relieved; gained 3 ounces. Quality and quantity of food unchanged. Atropin, 1:2,000 given in each feeding until the baby showed symptoms of returning tension and discomfort. Then 1:1,000 was given for several feedings, controlling the condition entirely. In five days the baby gained 9 ounces; temperature 98.6 to 99 F. There was one large, digested stool daily, though still being passed with great effort and

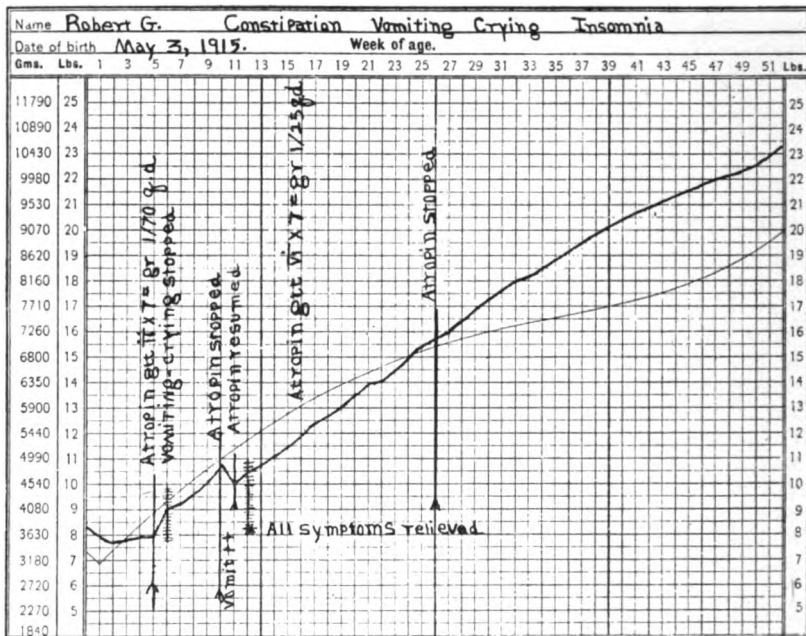


Chart 3 (Case 3).—Weight chart of Robert G.

some crying. The baby's whole expression changed; it looked comfortable; slept most of the time; extremities warm. From birth until starting the atropin treatment the baby's hands and feet were always cold unless especially covered with extra blankets and with hot water bottles in the crib.

Chart 2 (Case 2).—John M., born Nov. 12, 1915; weight 7½ pounds. Complaint, insomnia, crying and constipation. Jan. 12, 1916, first visit; aged 2 months; weight 9½ pounds; first baby; labor normal.

Diet: (1) Breast milk; (2) milk, limewater, lactose, water; (3) condensed milk; (4) malt soup.

New Diet: Imperial granum, water, maltine, whole milk; 2 drops of atropin in each bottle. Ten days after new régime was started there was a gain of 1 pound; general condition ++.

Oct. 26, 1916, aged 11 months; weight 22½ pounds; stopped atropin at 5 months; stopped maltine at 9 months. The child did well after atropin was begun.

Chart 3 (Case 3).—Robert G., born May 3, 1915; physical condition apparently good; weight 8½ pounds. Complaint, constipation, vomiting, crying and insomnia.

May 15, 1915, first visit, aged 12 days; weight 7 pounds 13 ounces.

Feeding: (1) Breast milk; (2) breast feeding and sodium citrate; (3) malt soup; (4) Schloss milk; (5) modified cow's milk. Paregoric was used for the crying and sleeplessness, without result.

June 15, 1915, atropin, 2 drops in each feeding; weight, 8.1 pounds.

June 22, 1915, weight 8.15 pounds; symptoms absent.

July 15, 1915, atropin stopped four days previously with return of symptoms.

Aug. 27, 1915, 4 months old; weight 11.14 pounds; occasional vomiting.

Dec. 4, 1915, 7 months old; weight 17.4 pounds; atropin stopped at sixth month; no symptoms.

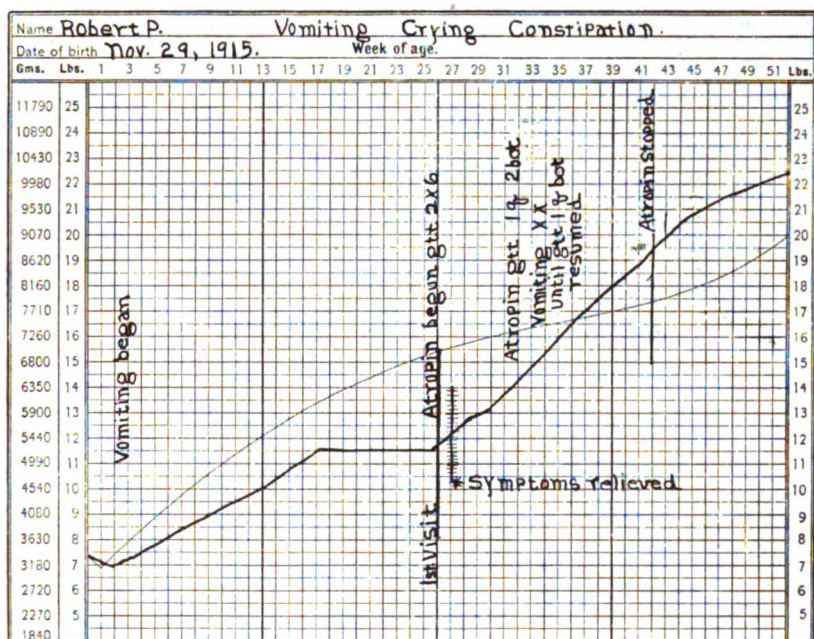


Chart 4 (Case 4).—Weight chart of Robert P.

Chart 4 (Case 4).—Robert P., born Nov. 1, 1915; weight 7.5 pounds; second child; labor normal. Complaint, vomiting, crying and constipation.

Feeding: (1) Breast and condensed milk two and a half months; slight gain; no vomiting; (2) top milk, granum, malt soup; curds, mucus and diarrhea; (3) barley, with skimmed milk; irregular gain; (4) granum, evaporated milk, lactose; (5) aqua cakes, water, lactose, milk. Began to vomit at three weeks (projectile), and has continued up to the present.

May 25, 1916, first visit; aged 6 months; weight 11.10 pounds; atropin, 2 drops in each bottle. New Diet: Granum ½ ounce, maltine ½ ounce, milk 20 ounces, water 16 ounces, divided into six bottles.

May 31, 1916, weight 12.3 pounds; symptoms absent.

July 24, 1916, occasional projectile vomiting; weight 16 pounds; 8 months old.

Several attempts to stop atropin resulted in a recurrence of symptoms within forty-eight hours. At the age of 25 months the weight was 29½ pounds; height 34 inches.

Chart 5 (Case 5).—(Referred by Dr. A. W. Roff.) George H. S., born March 24, 1915; birth weight 9 pounds.

Complaint, insomnia, constipation, vomiting, crying and visible peristalsis. Second child; labor normal; present weight 8.15 pounds.

Feeding: (1) Breast three weeks; (2) condensed milk; (3) Horlick's malted milk; (4) granum; (5) modified milk; first visit (6) modified milk, fat $2\frac{1}{2}\%$, protein $\frac{1}{2}\%$, granulated sugar 6; May 12, 1915, (7) modified milk, fat 1%, protein 1%, dextro-maltose 6; 3 ounces every two and a half hours.

May 18, 1915, stool improved; vomiting severe; other symptoms not improved; weight 9.8 pounds; atropin started, 5 drops before each feeding.

May 19, 1915, no vomiting; quiet, but constipated; lips and throat dry; atropin reduced to 2 drops.

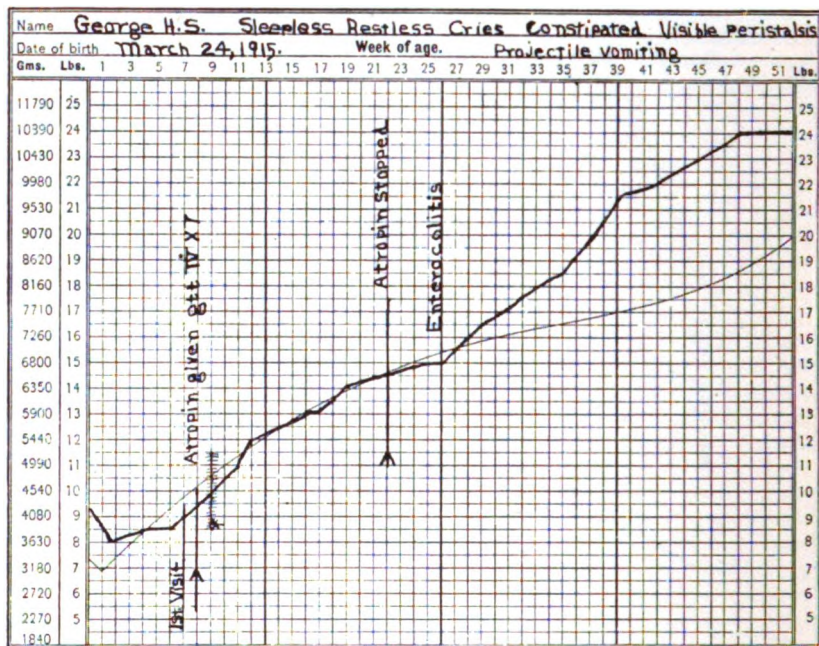


Chart 5 (Case 5).—Weight chart of George H. S.

June 26, 1915, appearance, good; slight sign of rickets; vomits infrequently; sleep improved but cries and is constipated. Atropin stopped and paregoric, 12 drops, given in each feeding. This apparently had no effect. All symptoms returned. When atropin was used, it seemed to warm and quiet him.

July 23, 1915, weight $13\frac{1}{2}$ pounds.

Formula: Milk 26, barley water 8, limewater 2, dextro-maltose $2\frac{1}{2}\%$; $6\frac{1}{2}$ ounces, seven feedings. Received atropin, 4 drops at each feeding; could not get along on less; peristalsis visible at times; other symptoms practically absent, excepting those of rickets, which were slow in clearing up.

Atropin taken more or less constantly until the child was 1 year old.

Chart 6 (Case 6).—(Through courtesy of Dr. W. M. Stone.) Grace G., born May 19, 1916; second child; first died in labor; birth weight 5.8 pounds. Complaint, irritability, crying, vomiting and slight constipation.

Feeding: (1) Breast, two weeks; weight dropped to 4.10 pounds the first week; (2) barley water, limewater; present formula (3), milk 7, limewater 1,

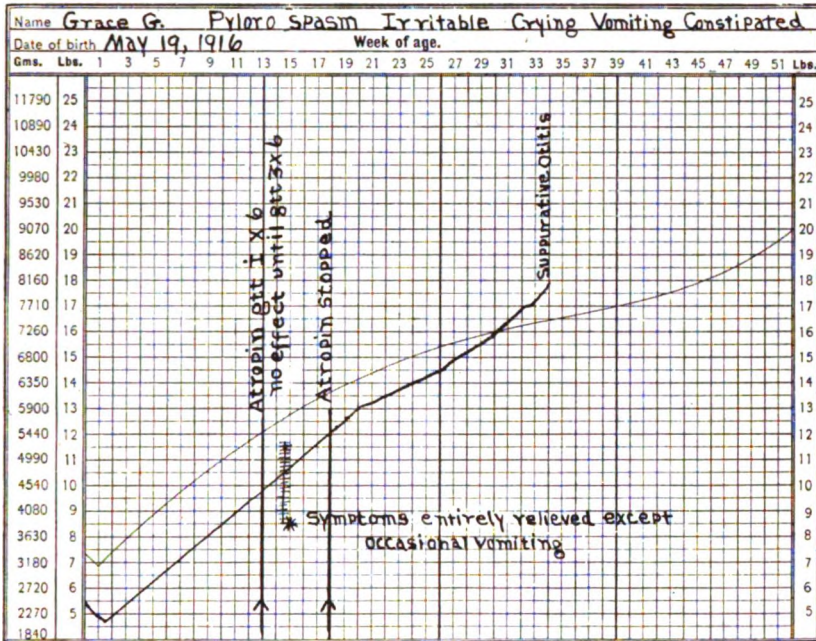


Chart 6 (Case 6).—Weight chart of Grace G.

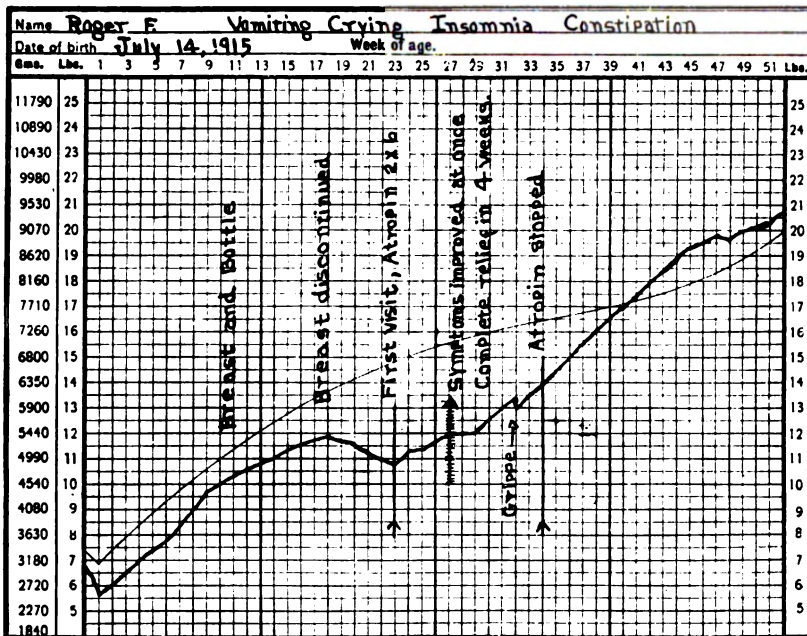


Chart 7 (Case 7).—Weight chart of Roger F.

cane sugar 2, barley water 12; 4 to 6 ounces every four hours; peptonized; peanut oil 1 drop fifteen minutes before feeding.

First visit, Aug. 16, 1916, weight 9.6 pounds; pale; abdomen shows peristalsis; stands with support; atropin, 1 drop in each feeding.

Aug. 25, 1916, symptoms relieved entirely, excepting the vomiting, which was not entirely eliminated; no effect from less than 3 drops of atropin solution.

Formula: Milk 12, dextro-maltose 2, limewater 1, barley water 10.

Sept. 1, 1916, milk 15 ounces, dextro-maltose 2, limewater 1, barley water 9. Vomits about once a week; other symptoms absent.

Infant at present is peculiar and unsocial.

Chart 7 (Case 7).—(Referred by Dr. J. T. Simonson.) Roger F., born July 14, 1915; birth weight 6.10 pounds. Complaint, vomiting, crying, insomnia and constipation; no gain recently.

Previous Feeding: (1) Breast; (2) breast, barley water (3 months); (3) breast, top milk 9½, dextrinized barley water 10½ (fourth month); (4) top milk 8 ounces; barley water; (5) top milk 24 ounces; (6) skim milk; (7) milk, sugar, water; (8) condensed milk 1:10; (9) top milk mixture peptonized; (10) malt soup; (11) protein milk.

SUMMARY OF CASES

Case	Name	Con- stipation	Vomit- ing	Insom- nia	Cry- ing	Peris- talsis	Los- ing	No Gain	Under Wt., Pounds	Age When First Seen	Atropin Begun	Atropin Stopped
1	George S.	+	4th wk.	+?	+	+	..	+	1	7 wks.	5/ 8/15	8/24/15
2	Robert G.	+	2d wk.	+	+	..	+	..	1	5 wks.	6/ 8/15	11/ 5/15
3	Roger F.	+?	Early	+	+	..	++	..	4	5½ mos.	12/23/15	3/18/16
4	John M.	+		+	+	..	..	Slow	1	8 wks.	1/12/16	4/16/16
5	Robert P.	+	8d wk.	+	..	+	..	+	4	6 mos.	5/26/16	10/ 9/16
6	Grace G.	+	8th wk.	+?	+	..	..	Slow	3	18 wks.	8/16/16	10/22/16
7	Edward R. ...	+	4th wk.	+	+	+	..	+	1½	5 wks.	5/24/17	11/27/17

First visit, Dec. 23, 1915, aged 5½ months; weight 11 pounds; marked rickets. Prescribed full milk, 20 ounces, granum ½ ounce, maltine ½ ounce, water 16 ounces, 9 ounces every four hours; atropin, 2 drops in each feeding.

Dec. 28, 1915, appearance good; sleeps well; is comfortable; some spitting; constipation.

Jan. 28, 1916, symptoms entirely relieved; only slight gain. Weight 9.12 pounds. Was now put on a straight milk formula: milk 30, lactose 1, barley water 5, limewater 2.

Feb. 5, 1916, weight 12.10 pounds.

March 28, 1916, aged 8½ months; weight 15.8 pounds; no symptoms; atropin stopped ten days previously.

SUMMARY

The hypertonic infant shows a tendency to rigidity, overaction of involuntary muscles and soon after birth develops signs of physical and psychic irritation, presenting the syndrome (physical) of vomiting, often visible peristalsis, constipation and imperfect nutrition; (psy-
chic) of general irritability, insomnia and crying.

The etiologic factor of this state would appear to be a hyperexcitability of the autonomic nervous system.

Although apparently a feeding problem, changes in method and character of feeding does not correct the condition.

Atropin in doses of 1 drop or more of a 1:1,000 solution with each feeding usually relieves the condition at once and apparently increases the infant's tolerance for milk.

Atropin in these cases may be used in large doses without danger.

Investigation along these lines may reveal the etiology of hypertrophic pyloric stenosis.

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A STUDY OF THE EFFECT OF HUNGER ON NERVOUS IRRITABILITY *

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During a summer vacation one of us (R. G. H.) observed that a fat, lazy, overfed dog, after having been lost for three days, returned thinner, brighter and more alert and active in every way. At this time A. J. Carlson in his work on the physiology of hunger suggested that gastric contractions were associated with some increase in general nervous irritability. Zybelle's¹ clinical studies on spasmophilia also have a bearing on this subject. He concluded that any prolonged hunger aggravates the condition. He cast doubt on the idea that spasmophilia might be attributed to any specific element in the milk mixture, as the whey, the carbohydrate, or the starch additions, and demonstrated that independent of the nature of the food, a period of hunger prolonged over a few hours made the child decidedly worse. Indeed, he went even farther by showing that in spasmophilia the electrical reactions vary sometimes 1 to 2 milliamperes from morning to evening. These differences are due to the effect of hunger. The child, going through the night with very little food, awakens in the morning with pathologic reactions. After the day's feeding electrical irritability becomes normal. By changing the routine, by feeding through the night and giving very little food during the day, Zybelle was able to reverse the reaction.

From these studies and observations one is tempted to advance the hypothesis that there is a general law in nature making increased nervous irritability coincident with increased hunger. If this were so, it could possibly be demonstrated in mathematical form by means of the electric current. This we attempted. Our first work was with infants, but the tendency of the electrodes to burn the skin, the restlessness of the children making accurate readings difficult, and our own reluctance to subject the children to any prolonged starvation, led us to transfer the work to dogs.

Perhaps the most extensive researches in animals on the subject of electrical excitability are those of Noel Paton² and his associates. These observers, in the course of their work on parathyroid tetany, demonstrated (*a*) the extreme variability of the reactions, and (*b*) the sensitizing effect of the current, namely, that a nerve after once

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* From the Departments of Pediatrics and Physiology of the Northwestern University Medical School, and the Sarah Morris Hospital for Children.

1. Zybelle: *Jahrb. f. Kinderh.*, 1913, **28**, 29.

2. Paton, N.: *Quart. Jour. Exper. Physiol.*, 1916, **10**, 203.

reacting becomes sensitized, and then reacts to about one-half to one-quarter of the primary stimulus.

The problem which we thought could easily be settled in a few weeks lengthened to almost two years. During this time we learned much about electrical reactions, particularly the difficulty of obtaining *any sort* of definite standard. In a normal dog, even at best, the reactions show extreme variability, changing not only day by day, but sometimes almost minute by minute. During moist days the atmosphere seemed to induce currents in the electrical machine; on other days small deflections in the needle could be traced to the iron work in the building, electrically charged for some unknown reason. To hold animals quiet for any length of time is difficult, and one is often



Period A, change of hygiene of kennels; Period B, three days' starvation; Period C, four days' starvation. AO, anode opening; AC, anode closing; CC, cathode closing. The readings were all taken in the morning, except on the twenty-fourth day when a. m. and p. m. observations were made.

confused as to whether the muscular contraction is due to the current, to shivering, or is voluntary. Then again, dogs vary in temperament, some being exceedingly nervous, irritable and timid, while others are calm and make quiet subjects. Due to these many and often uncontrollable variables, we threw out repeatedly whole series of observations; at times we even despaired of obtaining any definite result. A few experiments were carried out successfully, however, and the accompanying curve may be taken as illustrative of some of the series.

The technic of these experiments was that ordinarily employed in obtaining the reactions in children. In order to be sure that the animals were experiencing the true hunger effects, we controlled their weight and temperature.

DISCUSSION

In studying the chart, particularly AOC, which observers have found the most constant, one finds some increase in the electrical excitability during the hunger periods, but we have learned of so many variables, and have plotted so many curves which do not show this increase, that we do not feel justified in asserting this as a definite law. That there is no direct *parallelism* between electrical excitability and duration of the hunger period, or between the former and the weight curve, however, is certainly shown by the p.m. reading of the twenty-fourth day. Here the animals had been on a full diet for six hours; the weight curve took a sharp rise, but the curve of electrical excitability went down. At no time, in spite of the severity of the hunger and the drop of weight, did starvation bring COC anywhere near 5 milliamperes. Thus we believe hunger to be of no great practical importance in predisposing a normal individual to spasmophilia. We believe the general subject of hygiene to be more important. During the first few days the dogs were confined in dark, unpleasant kennels; their appetites were poor and they were unhappy. At A they were placed in pleasanter quarters, were allowed freedom, fresh air, exercise and sunshine. It will be seen that during the period C, after four days' starvation, the reactions are barely lower than in the pre-starvation, poor hygiene days.

CONCLUSIONS

We were not able by means of the electric current to demonstrate in all cases a constant parallelism between the length of the hunger and the degree of *electrical* irritability. This latter seems to be influenced more by general hygiene, conditions of the kennels, exercise, sunshine, appetite and body weight than by the hunger factor alone. Perhaps the parallelism may be demonstrated by psycho-analytical methods. We certainly can confirm the work of Noel Paton and his associates as to the extreme variability of these reactions and the sensitizing effect of the electric current. This latter observation may be of clinical value. One should never be satisfied with a first reading. The observation should be repeated several times; often a contraction will be obtained by one half to one fourth the original stimulus. The failure of the COC even after four days' hunger nearly to approach 5 milliamperes leads us to conclude that hunger can scarcely be a factor in predisposing normal individuals to spasmophilia.

We wish to express our thanks to Dr. O. T. Schultz for the privileges of the laboratories of the Nelson Morris Memorial Institute, and to Mr. E. L. Berry of Northwestern University Medical School for his technical assistance.

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CLINICAL DEPARTMENT

THE TREATMENT OF ENURESIS WITHOUT DRUGS

WITH A REPORT OF THIRTY-FOUR CONSECUTIVE RECOVERIES *

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Enuresis may be caused by organic diseases and by malformations. The present discussion, however, has to do only with the incontinence of urine ordinarily seen in childhood.

In order to understand the treatment of this condition, it is necessary to know so far as possible the physiology of normal urination. This was described by Goltz¹ in 1874, and the general principles set forth by him at that time have continued to be accepted with little modification. Stated in its simplest terms, the act of micturition may be described as follows:² Gradual distention of the bladder induces rhythmic contraction of its walls. This contraction increases until a few drops of urine are expressed into the posterior urethra, causing a sensory stimulus, the afferent part of the reflex, which, passing to its nerve center in the lumbosacral cord, arouses the afferent impulses by which the bladder is made to contract vigorously and the sphincter to relax. This mechanism is, however, almost completely under the control of the will, so that micturition may be made to begin before the bladder is full, and, on the other hand, the action of the reflex may be prevented by a voluntary exercise of will power. This urinary reflex is of such a primitive character that it persists even after section of the spinal cord.

In infants, it can be excited by almost any irritation of the pelvic organs, thereby causing involuntary micturition.

Infants may begin to acquire control of this mechanism during their waking hours at the end of the first year. If they do not gain control during the third year, incontinence may be said to exist.

Enuresis in children is, then, not a disease, but simply the persistence of an infantile condition, or habit. Why this habit persists in

* Submitted for publication Jan. 15, 1918.

* Read at a meeting of the New England Pediatric Society, Boston, Dec. 14, 1917.

1. Goltz: Arch. f. d. ges. Physiol., 1874, 8, 478.

2. Starling, E. H.: The Principles of Human Physiology, 1915.

one child and not in another has furnished a fertile field for speculation without furnishing a satisfactory solution.

The following affections have been considered possible causes of this condition :

Anemia	Tuberculosis	Distant organs as the nose,
Malnutrition	Enteritis	throat and eye
Heredity	Rheumatism	Adherent prepuce or clitoris
Neurasthenia	Malaria	Hyperacidity of the urine
Chorea	Syphilis	Alkalinity of the urine
Epilepsy	Uric acid diathesis	High specific gravity
Hysteria	Rachitis	Low specific gravity

The mere enumeration of this large number of affections is evidence that the real cause has not been found. In this series of cases the treatment of no one of these affections mentioned has relieved enuresis.

In a group study of 100 children reported by the writer³ during the present year, no special incidence was found of enuresis with adherent prepuce or clitoris, mental retardation, carious teeth or malnutrition. There was, however, marked incidence with nasopharyngeal obstruction. These observations are verified by the study of a second group of 100 children which give almost identical results.

Many drugs have been used for the treatment of enuresis, but no specific has been discovered. Those most frequently given are :

Citrate and acetate of potash	Hexamethylenamin	Bromids
Benzoate of soda	Strychnin	Thyroid extract
	Hyoscyamus	Belladonna

The children included in the series of thirty-four cases presented in this paper all recovered without the use of any drugs whatsoever.

In discussing the following method of treatment the expressions "wet habit" and "dry habit" are used. By "wet habit" is meant the infantile condition where the reflex acts more or less normally, but the mind of the child is unconscious of the sensory impulse or else disregards it. By "dry habit" is meant the child perceives the sensory impulse and his will acts to control the reflex. The following treatment is directed toward teaching the child the "dry habit" and, on the other hand, of interrupting and eliminating the "wet habit."

This treatment may be considered to consist of four methods, all or one of which may be used in a given case to establish the "dry habit." The "dry habit" once inaugurated must then be continued by careful oversight.

3. Emerson, William R. P.: A Group Study of the Results of One Hundred Physical and Mental Examinations of So-Called Well Children, *Internat. Clin.*, **11**, Series 27.

First Method.—Mental suggestion. This consists of arousing the patient's interest and attention to the act by rewards and other mental suggestions. This method of treatment is entirely adequate to relieve about 40 per cent.⁴ of all cases of enuresis. It is this mild class of cases so relieved that are supposed to have reacted to the use of drugs, particularly to atropin, because in giving atropin, the patient is seen repeatedly, and, more or less unconsciously suggestion is used over a considerable period of time.

TABLE 1.—SHOWING INCIDENCE OF EIGHTEEN CASES OF ENURESIS WITH OTHER CONDITIONS, OCCURRING IN A GROUP OF 200 CHILDREN

No.	Patient	Naso-pharyngeal Obstruction	Mouth Breathers	Under-weight	Adherent Prepuce	Mental Retardation	Carious Teeth
6	M. H.	+	+	..	..	+	+
13	S. M.	+	+	..	+	..	+
7	F. B.	+	+	..	..	..	..
12	B. B.	+	+	+	..	+	+
8	B. C.	..	+	..	..	..	+
24	J. M.	+	+	..	..	+	..
11	G. K.	..	..	..	..	..	..
9	M. H.	+	..	..	..	..	..
10	E. A.	+	..	..	..	..	+
15	H. McK.	+	..	+	+	..	..
16	F. S.	+	+	..	..	..	..
19	I. S.	+	+	..	..	..	+
18	L. Y.	+	+	..	+	..	..
19	T. S.	+	+	..	..	+	+
20	N. S.	+	+	+	..	..	+
21	O. S.	+	+	..	..	..	+
22	E. S.	+	+	..	..	+	+
23	F. B.	+	+	+	+	..	+
		16 cases 88 per cent. (100 group 67 per cent.)	14 cases 77 per cent. (100 group 62 per cent.)	4 cases 22 per cent. (100 group 22 per cent.)	4 cases 22 per cent. (100 group 19 per cent.)	5 cases 28 per cent. (100 group 40 per cent.)	11 cases 61 per cent. (100 group 64 per cent.)

Second Method.—Establishing the Dry Habit. This is accomplished by teaching the reflex to act at regular intervals, and always before the time the "wet habit" occurs. In this way the patient is always dry. The periods of urinations are gradually lengthened. By such systematic training the mechanism of urination soon acts under

4. True in a series of eighteen cases of enuresis occurring in a group of 200 children.

the patient's control and the "dry habit" is established. This method is described by Newlin⁵ as "The simple procedure of anticipating the involuntary by a voluntary emptying of the bladder."

Third Method.—Local irritation. This is brought about by irritating the vesicular sphincter and the posterior urethra by means of a bougie-a-boule, so that sensory impulses passing to the brain will become intensified sufficiently to attract the patient's attention, until the habit of control is attained.

A bougie-a-boule should be used under antiseptic conditions. It should be introduced along the posterior urethra into the bladder without pain. It should be withdrawn through the sphincter, then passed in and out about four times, sufficiently to cause a sensation of discomfort during the next few urinations. This sensation of discomfort in urinating brings the act into the child's consciousness, aiding him in control. The idea of this treatment was suggested by the report of a patient who was relieved after the passing of a sound, and also by the fact that most children with enuresis are entirely unconscious of the act of urination. They waken at night and find themselves wet.

Fourth Method.—Cerebrospinal irritation. This is produced by the injection into the spinal canal of physiologic sodium chlorid solution, producing such stimulation as to arouse the whole mechanism into consciousness when habit holds it under control. This procedure should be carried out exactly as for lumbar puncture. A small trocar should be used with cocain analgesia. Ten c.c. of spinal fluid are withdrawn and 12 c.c. of freshly prepared physiologic sodium chlorid solution introduced into the spinal canal. The child should then be kept in bed at least six hours. There is apt to be some reaction, namely, headache and nausea, unless the saline solution is prepared from freshly distilled water and then filtered. This method of treatment is necessary only in extreme cases of enuresis, or those complicated by mental deficiency. It should be used only after other treatment fails; even then the question arises whether lumbar puncture is justified for such a comparatively simple condition as enuresis. It should be borne in mind, however, that enuresis after puberty is not a simple condition. It affects that which most of all makes life worth living, association with other human beings. When combined with incontinence of feces, as in three of the cases reported, the question is not debatable. Good foster-homes, summer camps and schools refused certain of these children because of enuresis. The brothers and sisters of one boy turned against him because he was constantly

5. Newlin, Arthur: The Management of Enuresis, Arch. Pediat., 1916, **32**, No. 10.

wet with urine. To the sensitive child this condition of incontinence may almost amount to a tragedy.

These methods singly or combined, have been sufficient to relieve the thirty-four children in the following series. This series includes all children to whom there was opportunity to give complete treatment. For convenience of reference the cases are reported according to their reaction to these four methods.

REPORT OF CASES

GROUP 1.—Recovery brought about by mental suggestion. This group includes Cases 6 to 11, 13, 14 and 34—nine cases. These children presented nothing in their history out of the ordinary in such conditions.

Marion M., aged 5, No. 6, was being treated for vulvovaginitis, but the enuresis preceded this affection.

Fred R., aged 9, No. 7, was punished by an irate matron, with temporary improvement, but complete recovery was brought about by encouragement and rewards. This may be explained by the fact that rewards stimulate the attention, while punishment introduces the element of fear, which is repression.

GROUP 2.—Recovery brought about by establishing the "dry habit." This group includes Cases 18 to 25, 29 and 30—ten cases—four boys and six girls. These all failed to respond to mental suggestion. They were wet almost constantly at night. Cases 18, 22 and 24 were wet also during the day. All had been afflicted with this condition since birth. Their ages varied from 5 to 11 years. The three diurnal cases were sent to the toilet every hour during the first day and all cases every hour the first night until midnight, then every two hours until morning. The second day these periods were lengthened to one and one-half hours and the third day to two hours. In the majority of these cases the "dry habit" was established by the end of the week, the child going to the closet or using the chamber of his own accord when necessary. Four of these children had a certain hour when wetting occurred, two about one-half hours after being put to bed, and two children at 2:30 in the morning. These children were taken up shortly before these times, and it was necessary that this be continued longer than for those who did not have established periods for wetting. In the treatment of these cases an alarm clock was useful for wakening, especially for older children.

GROUP 3.—Recovery brought about by local irritation.

Lillian H., aged 13, No. 28 (B. Inf.),⁶ had nocturnal enuresis all her life. A soft catheter, French, No. 15, was introduced into the bladder with little lubrication. It was then moved to produce slight irritation and withdrawn. Report four weeks later, no enuresis since treatment.

Hita F., aged 3, No. 31 (M. G. H.),⁶ wet herself continually at night. A bougie-a-boule, size 9, was passed along the posterior urethra and through the vesical sphincter into the bladder sufficiently to produce irritation. The child reported at the end of a week, "I wet my bed no more." She asks for the chamber two or three times at night and keeps herself entirely dry. The mother of this child had enuresis until puberty.

Gertrude N., aged 14, No. 32 (B. Inf.), had enuresis since birth. A catheter, No. 12, French, was passed Nov. 19, 1917. Report thirteen days later, no enuresis since treatment. This patient had chorea in 1916.

Ernest H., aged 13, No. 33 (B. Inf.), had enuresis since birth. Even if awakened twice at night he would still be wet. Nov. 17, 1917, a bougie-a-boule No. 12 was passed. Twenty-seven days later the report was, no enuresis.

6. B. Inf. Berkeley Infirmary: L. W. H., New England Home for Little Wanderers; M. G. H., Massachusetts General Hospital.

TABLE 2.—GROUP 1. MENTAL SUGGESTION

No.	Name	Age	Diurnal	Nocturnal	Recovered	Follow-up Report	Remarks
7	Fred B.	9	..	+	+	6 mos.	Liquids restricted; regular habits
6	Marion M. ...	5	..	+	+	6 mos.	Regular habits; pride; rewards; vulvovaginitis
8	Russ C.	9	..	+	+	1 yr. +	Liquid restricted; regular habits
9	Mary H.	16	..	+	+	1 yr. +	Regular habits
11	Gordon K. ...	7	..	+	+	1 yr. +	Regular habits
10	Ethel A.	7	..	+	+	1 wk.	Rewards; regular habits
13	Samuel M. ...	6	..	+	+	1 yr.	Regular habits
14	Edward B. ...	10	..	+	+	1 yr.	Regular habits
34	James M.	9	..	+	+	3 wks.	Regular habits

TABLE 3.—GROUP 2. "DRY HABIT"

No.	Name	Age	Diurnal	Nocturnal	Recovered	Follow-up Report	Remarks
18	Louis Y.	5	+	+	+	1 wk.	Vulvovaginitis
19	Thelma S. ...	11	..	+	+	3 mos.	
20	Norma S.	9	..	+	+	3 mos.	
21	Ola S.	7	..	+	+	3 mos.	
22	Edna S.	6	+	+	+	3 mos.	
23	Freeman B. ..	6	..	+	+		
24	Lester B.	7	+	+	+	1 yr.	Thyroid-Saline 6 c.e.
25	Lillian H.	7	..	+	+	3 wks.	Alarm clock 2 a. m.
29	Charlotte B.	5	..	+	+	15 mos.	
30	Barbara B. ..	4	..	+	+	15 mos.	

TABLE 4.—GROUP 3. LOCAL IRRITATION

No.	Name	Age	Diurnal	Nocturnal	Treatment	Follow-up Report	Remarks
25	Lillian H.	11	..	+	+ Cath. No. 12	3 wks. +	One treatment
31	Eita F.	8	..	+	+ Bougie No. 9	3 wks.	Mother had enuresis until puberty; one treatment
32	Gertrude M.	14	..	+	+ Cath. No. 12	13 days	Chorea 1916; 2 treatments
33	Ernest A.	13	..	+	+ Bougie No. 12	10 days +	Three treatments

In each of these cases this treatment was followed up by regular habits of urination, limited liquids and dry supper at night. As in Groups 1 and 2, each child was awakened at about 10 p. m. for urination and encouraged by mental suggestion to form the "dry habit." The report of this group is a preliminary one only, as it has been tried in too few cases to ascertain its true value.

GROUP 4.—Recovery brought about by introducing physiologic sodium chlorid solution into the spinal canal.

TABLE 5.—GROUP 4. SPINAL INJECTION

No.	Name	Age	Enuresis		In- conti- nence of Feces	Num- ber C.c.*	Anes- thetic	Reac- tion	Recov- ered	Report	Remarks
			Diur- nal	Noc- turn- al							
1	John F.	6	+	+	+	10— 10+	None	None	+	6 mos.	
2	Francis H.	12	+	+	+	9— 10+	Ether	++	+	1 yr. +	"Psycho- pathic"; "erratic"; police
3	John M.	13	+	+	..	18— 10+	Ether	None	+	1½ yrs.	Refused summer camp
4	Thomas F.	4	+	+	..	10+	Ether	++	+	2 yrs. +	Mentally de- ficient
5	Francis McL.	7	..	+	..	10— 10+	Ether	None	+	1 yr. +	Lazy
12	Bertram R.	12	..	+	..	10— 10+	Ether	None	+	1 yr.	
15	Hector McK.	5	+	+	..	10— 10+	Cocain	+	+	2 wks. +	Mumps; ad- herent pre- puce
16	Frank S.	4	+	+	..	10— 10+	Cocain	+	+	2 mos. +	Mumps
17	Irene S.	4	+	+	..	10— 10+	Cocain	+	+	2 wks. +	
26	Barnard W.	19	+	+	..	10— 12+	Cocain	None	+	6 mos.	Septum op- eration re- fused; lodg- ings
27	Hilda A.	11	+	+	+	10— 12+ 12+	Cocain	None	+	6 wks. +	Mentally de- ficient; re- fused sch'l

* The minus sign marks the amount of spinal fluid withdrawn and the plus sign the amount of saline solution introduced.

John F., Italian, aged 6, earned pennies by dancing in the public market. This boy had both incontinence of urine and feces. He was admitted to the Boston Dispensary Hospital for Children, April 4, 1913. The first night he passed both urine and feces in bed. The next day lumbar puncture was performed without anesthetic, 10 c.c. of spinal fluid being replaced by 10 c.c. of physiologic sodium chlorid solution. He had no more incontinence while in the hospital, eleven days, and was reported to have none six months later.

Francis H., aged 7, No. 2 (B. Inf.), reported by the Psychopathic Hospital as not mentally deficient, but erratic. He was truant and had trouble with the police. He had incontinence of both urine and feces. His bowels would move when he was 10 feet from the toilet without his paying any attention to the act.

He was wet almost constantly. In 1913, 10 c.c. of spinal fluid were replaced by 10 c.c. of physiologic sodium chlorid solution. He gained control of his bowels at once, but continued to have enuresis. Two years later the spinal treatment was repeated under ether. This treatment was followed by marked reaction, headache, vomiting and temperature of 103 F. The reaction passed off in twenty-four hours. It seemed probable that it was occasioned by the use of solution not absolutely fresh. He reported in 1917, no further incontinence since last treatment.

John M., aged 12, No. 3 (B. Inf.), had enuresis since birth. Wet every night. He had been given various treatments with no effect. Ten c.c. spinal fluid were replaced by 10 c.c. of physiologic sodium chlorid solution under ether. No reaction. Report eighteen months later, no enuresis since treatment.

Thomas F., aged 4, No. 4 (B. Inf.), was mentally deficient. Wet day and night, almost every hour. Ten c.c. of spinal fluid were replaced by 10 c.c. physiologic sodium chlorid solution. Marked reaction; headache; vomited five times; temperature 101 F. This reaction passed off in six hours. He reported after two years, November, 1917, no enuresis since treatment.

Francis L., aged 7, No. 5 (B. Inf.), had enuresis since birth. Ten c.c. of spinal fluid were replaced by 10 c.c. of physiologic sodium chlorid solution. Report eighteen months later, no enuresis since treatment.

Bertram R., aged 12 (L. W. H.),⁸ wet every night. Ten c.c. of spinal fluid were replaced by 10 c.c. of physiologic sodium chlorid solution. No enuresis while in the home, about four months.

Hector M., aged 5, No. 15, had enuresis every night. December, 1916, he was given "dry habit" treatment with good results. He was dry a whole week; then he was sent to the City Hospital with mumps and returned with a relapse of the enuresis habit. March, 1917, 10 c.c. of spinal fluid were replaced by 10 c.c. of physiologic sodium chlorid solution. There was some reaction for six hours, with headache and nausea. Since treatment the child goes to the toilet of his own accord. Report some months later, no enuresis.

Frank S., aged 4, No. 16 (L. W. H.), had enuresis day and night. He was treated by the second method with good result. January, 1917, he was sent to the City Hospital with mumps; returned wet every night. March, 1917, 10 c.c. of spinal fluid were withdrawn and 12 c.c. physiologic sodium chlorid solution were introduced. There was a reaction for about six hours, with headache and nausea. Report two months later, no enuresis.

Irene S., aged 4 (L. W. H.), had enuresis day and night. She wet herself during the day while sitting up in bed. She was taken to the toilet regularly, with no effect. Ten c.c. of spinal fluid were withdrawn and 12 c.c. of physiologic sodium chlorid introduced into the spinal canal. Some reaction occurred with nausea and headache for about six hours. Reported sixteen days following, goes to toilet of her own accord and has no enuresis.

Bernard W., aged 19, No. 26, was referred from the Psychopathic Hospital. Wet since birth; for the previous two years only two or three times a week. On account of his incontinence the average boarding house would keep him about four weeks. He considered himself a wanderer on the face of the earth and therefore earnestly desired treatment. His enuresis occurred regularly at about 2:30 in the morning. He was told to set an alarm clock at 2 a. m. This wakened the boarders, but not the patient. In April, 1917, 10 c.c. of spinal fluid were withdrawn and 12 c.c. of physiologic sodium chlorid solution introduced. Report three months later, no enuresis.

Hilda A., aged 11, No. 27, was referred from Jamaica Plain Children's Aid Society. Mentally deficient; incontinence of both urine and feces since birth; wet herself every one-half to three-fourths of an hour; expels gas from bowels without control; discharged from school on this account. July, 1917, 10 c.c. of spinal fluid were withdrawn and 12 c.c. of physiologic sodium chlorid solution introduced. Reported a month later, no incontinence of either bladder or bowels since treatment.

Just how the saline solution acts on the reflex in these cases is not clear. The effect was apparently the same when given under ether, cocain or without anesthetic. In two cases of dry tap and in two cases in which only 6 c.c. of physiologic sodium chlorid solution were introduced into the spinal canal there was no apparent effect on the enuresis.

657 Boylston Street.

XANTHOCHROMIA OF THE SPINAL FLUID WITH COMPLETE COAGULATION IN TUBERCULOUS MENINGITIS *

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During the last fifteen years the occurrence of xanthochromia (yellow discoloration) of the cerebrospinal fluid has been noted by several observers. Sprunt and Walker¹ have recently collected 100 examples from the literature which showed this condition. They have divided the cases with this variety of spinal fluid into two main groups: (1) those in which the color is due to dissolved hemoglobin or its derivatives; these fluids, as a rule, do not coagulate spontaneously and contain only a small amount of globulin; they are usually associated with tumors of the brain in contact with the meninges, or tumors originating in the ventricles; (2) the larger and more important group which comprise those cases showing the so-called "Froin syndrome." The fluid in this group is transparently clear, yellow, coagulates spontaneously and contains a large amount of globulin; it may or may not show pleocytosis, and it gives no positive reaction for hemoglobin.

Reviewing the cases recorded up to 1912, Mix² finds that whenever a spinal fluid conforms to the second group described it indicates that there is an isolated sac in the spinal subarachnoid space which has been shut off from communication with the ventricles of the brain. This condition may be due to (1) a meningitis which had caused adhesions between the meninges and the surface of the cord, (2) to a pachymeningomyelitis of the conus terminalis, or (3) to a tumor which compresses intradurally or extradurally. It always signifies organic disease.

REPORT OF CASE

History.—C. B., a boy, aged 9 months, was admitted to the Babies' Hospital, Aug. 23, 1917. The parents and one other child were healthy. So far as could be ascertained, there was no tuberculosis in the family. The baby was born at term and weighed 9 pounds. Fourteen days before admission he had a little fever and was more restless than usual. Four days later the head was retracted and he was so drowsy that he had to be aroused for his feedings. There had been no vomiting or convulsions, but he had considerable twitching movements during sleep.

* Submitted for publication March 11, 1918.

1. Sprunt and Walker: Bull. Johns Hopkins Hosp., 1917, **28**, 80.
2. Mix: Surgical Clinics of Chicago, 1915, **4**, 317.

Examination.—On examination the patient presented the typical picture of a tuberculous meningitis. He lay in a condition of deep stupor and slept most of the time. Even when aroused he took no notice of his surroundings. The head was slightly retracted, the fontanel full, and there were automatic movements of the arms and legs on both sides. The eyelids were half open and the eyes rolled continually from side to side. There was a coarse lateral nystagmus and an inconstant strabismus. The pulse and respirations were very irregular. The abdomen was not retracted; there was a marked '*tâche cérébrale*', and the liver and spleen were palpable at the costal margin. The extremities were moderately spastic and all the reflexes were exaggerated. The von Pirquet skin test was strongly positive.

The leukocytes in the blood numbered 10,000 per c.mm. of which 39 per cent. were polymorphonuclears and 61 per cent. were lymphocytes. A spinal puncture was made and 15 c.c. of fluid removed under low pressure. The fluid was slightly turbid and of a light amber color, resembling urine. The cells numbered 250 per c.mm., 76 per cent. of these being lymphocytes. Within ten minutes after withdrawal the fluid coagulated to a jelly-like mass, to such an extent that the tube could be inverted without spilling the contents.

For the next three days the drowsiness and prostration gradually increased. The spastic condition of the arms and legs continued but became more marked on the left side. Finally, there was a marked weakness of the left side of the face and a constant external strabismus of the left eye. The temperature ranged between 99 and 100 F. There was increased coma until death on the third day.

Necropsy.—At the postmortem examination made by Dr. Martha Wollstein, the brain and meninges showed the typical lesions of a tuberculous meningitis. The dura and pia mater were everywhere congested. Numerous miliary tubercles were present along the surfaces of both cerebral and cerebellar hemispheres. The lateral ventricles were slightly dilated and their floors peppered with miliary tubercles. Over the base of the brain there was an exudate of serum and fibrin covering the lower surface of the cerebellum, pons, medulla and extending over the island of Reil on both sides, causing marked thickening of the basal pia. The thickening of the meninges was very marked over the cervical cord. There were adhesions between the pia and dura along the upper 12 cm. of the cord, which is all that could be examined. The pia-arachnoid membrane measured on section nearly 0.5 cm. in thickness.

REMARKS

From the clinical picture, the von Pirquet reaction and the cytology of the spinal fluid it was evident that a tuberculous meningitis was present. The yellow color and massive coagulation of the spinal fluid, however, indicated that an obstruction existed somewhere in the spinal subarachnoid space. The spine was carefully examined but no evidence of Potts' disease was found.³ It was then inferred that a solitary tubercle of the cord or a tuberculous thickening of the spinal meninges⁴ probably existed.

The tubercle bacilli were not found in the yellow spinal fluid during life, but at the necropsy a clear, limpid fluid was obtained from the ventricles in which the bacilli were easily demonstrated.

3. Bromer: Am. Jour. Med. Sc., 1916, **151**, 378.

4. Hanes: Am. Jour. Med. Sc., 1916, **152**, 66.

In this case the thickening of the cervical membranes and the adhesions were quite sufficient to cause the obliteration of the subarachnoid space at this level. The spinal fluid in the lower portion of the canal was thus shut off from communication with the fluid in the ventricles above, and it is in similar conditions that the spinal fluid becomes yellow in color and coagulates spontaneously on removal.

I am indebted to Dr. L. Emmett Holt for the privilege of reporting this case.

PYLOROSPASM AND CONGENITAL PYLORIC STENOSIS

PROBABLY THE EARLIEST REPORTED CASE *

JOHN FOOTE, M.D.

WASHINGTON, D. C.

In 1788 Hezekiah Beardsley, an American physician, published a report of a "Case of Scirrhus in the Pylorus of an Infant," which Professor William Osler, in 1903, identified as "congenital hypertrophic stenosis of the pylorus." This case report was republished under its newer title in *Archives of Pediatrics* (1903, 20) with the following note by Professor Osler:

Cantley and Dent in a recent paper (*Lancet*, Dec. 20, 1902) state that the first record of this disease, which is now exciting a good deal of interest, dates back to 1841. The report here given by Dr. Beardsley of a very clearly and accurately described case, is, I think, worth republishing. It appears in the earliest volume of medical transactions issued in this country entitled, "Cases and Observations of the Medical Society of New Haven County in the State of Connecticut," New Haven, J. Meigs, 1788.

While Beardsley's monograph still stands as the first separate publication dealing with pyloric spasm and stenosis, the distinction of describing and actually naming with the term we now use the symptoms and pathology of this disease of the new-born apparently belongs to George Armstrong, an English pediatricist, whose work appeared in 1777, a textbook entitled "An Account of the Diseases Most Incident to Children from their Birth till the Age of Puberty, with a Successful Method of Treating Them, etc." (London, 1777). This textbook was accorded several reprintings, and was rewritten by Buchan in 1808. Clinical and post mortem findings, a typical case history, and a family history, including three similar cases, led Armstrong to conclude that a child which he had treated for "watery gripes" died from "*spasm of the pylorus*."

On page 49 of the edition of 1777 Armstrong, in discussing the reasons why antimonial emetics sometimes fail to produce beneficial results in intestinal diseases, has described a macerated or softened condition of the intestines seen in some fatal cases. He says:

In a child about 3 weeks old that died of the watery gripes, and which I opened some time since, I found most of the stomach toward the upper orifice and almost the whole fundus in the same tender state. But toward the pylorus the structure was firm enough as likewise that of the intestines, both small

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and great. The stomach was quite distended with curdled milk and victuals with which the nurse had crammed the child, mixed likewise with some of the chalk julep, but the whole intestines were remarkably empty. There were no morbid appearances to be observed anywhere but in the stomach, and this viscus being so full while the intestines were almost empty, it looked as if the disease had been chiefly owing to a *spasm in the pylorus*, which prevented the contents of the stomach from passing into the duodenum.

Perhaps cases of this kind are more frequent than is commonly imagined. . . . What is remarkable, this is the third child (and they had never had any more) which the parents have lost at the same age and with the same disease. And this was likewise the case in the family where the other died.

As to his term "the watery gripes," we find on page 20 that "vomiting and green stools" are the threatening symptoms which if allowed to continue "often end in convulsions and death."

The age of the child, "about three weeks," shows the development of vomiting during what we now recognize as the conventional period for the beginning of the disease. The citation of three other cases, two of them in the same family, occurring at the same period of life, shows that Armstrong believed that he had discovered a hitherto undescribed condition, though he says, very modestly: "perhaps cases of this kind are more frequent than is commonly supposed."

The stomach of a soft and flabby texture in contrast with the firm pylorus, and containing food "while the whole intestines were remarkably empty" leads him logically to his conclusion that "it looked as if the disease had been *chiefly due to a spasm in the pylorus*." He, however, omitted any comment on the intimate structure of the pylorus itself, being probably content with a physiologic rather than an anatomic explanation.

In the case reported by Beardsley as "Scirrhus in the Pylorus of an Infant," death occurred at the age of 5 years, after a history of malnutrition and vomiting beginning with the first week of life. The stools in Beardsley's case had always been "small in quantity and of an ash color," that is, free from bile pigment. Moreover, the gall-bladder was "nearly five inches in length and more than one in diameter, . . . its contents were rather solid than fluid and resembled flesh in a highly putrid state." Cholecystitis is not a usual condition in pylorospasm or pyloric hypertrophy of infants, and aside from Armstrong's priority of publication by eleven years, Beardsley's case is in this respect at least less true to type than Armstrong's.

It may not be out of place to add that George Armstrong organized the first and only hospital and dispensary for poor children in London in his day in the year 1769. It was here he made his therapeutic experiments and had opportunity to compare clinical records with the post mortem findings scattered so plentifully through his textbook. Here, too, he formulated his excellent "Rules for Nursing." It is a

sad commentary on the spirit of his day that after spending practically all his time and savings in building up the dispensary, he was forced to close it in the year 1781 for lack of financial support, although in the twelve years of its existence over 35,000 children had received treatment. This keen observer, brilliant writer and pioneer physician-philanthropist, who was blessed with the true scientific spirit and an almost prophetic outlook, died in obscurity, unpraised and unrewarded excepting in the grateful remembrance of the poor of London.

1726 M. Street N.W.

CONGENITAL INTESTINAL OBSTRUCTION, WITH THE REPORT OF A CASE *

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Although the standard works on embryology, anatomy, pathology and pediatrics seldom refer to the interesting condition of congenital obstruction of the small intestine, isolated case reports are not infrequent. In the large necropsy service of Bellevue Hospital during the past fourteen years, congenital obstruction of the intestine was encountered twice only.

Louise Cordes¹ collected fifty-six cases from the literature up to 1901, and reported a case of her own. Ballantyne,² in discussing the condition, says: "Antenatal narrowing or occlusion of the intestine is not very rare, but being an internal malformation, doubtless often escapes discovery." He reported a case with which he was acquainted and mentions the cases published by Durante³ (two cases), Jackson,⁴ A. Katz,⁵ and Kirmisson,⁶ not included by Cordes. Kirmisson's patient had been operated on for anal atresia soon after birth "with apparent success;" however, the infant died and necropsy showed a valvular obstruction of the duodenum, in addition to the anal defect. Spriggs⁷ gives an interesting account of twenty-four cases, with an excellent discussion and extensive references to the literature. Other cases of this condition as well as cases of congenital obstruction of the jejunum and cases of multiple obstructions have been reported. In an extensive search of the literature I have found a total of 143 cases of all kinds of congenital obstructions of the small intestine. The reader is referred to the appended list of references for details of these cases.

Kaufmann⁸ asserts that atresia of the small intestine is especially common at the point where the common duct joins the duct of Wirsung at its entry into the duodenum. Combinations of duodenal atresia with

* Submitted for publication March 12, 1918.

* From the Pathological Department of Bellevue and Allied Hospitals, Dr. Douglas Symmers, Acting Director.

1. Cordes, L.: Arch. Pediat., 1901, **18**, 401.

2. Ballantyne, J. W.: Manual of Antenatal Pathology and Hygiene, 1905; Tr. Edinburgh Obst. Soc., 1892, **17**, 133.

3. Durante: Bull. Soc. anat. de Paris, 1901, **76**, 593.

4. Jackson, J. B. S.: Boston Med. and Surg. Jour., 1858, **59**, 355.

5. Katz, A.: Bull. Soc. anat. de Paris, 1901, **76**, 471.

6. Kirmisson, E.: Traité des maladies chirurgicales, 1898, p. 412.

7. Spriggs, N. I.: Guy's Hosp. Rep., 1912.

8. Kaufmann, Eduard: Spezielle pathologische Anatomie, **1**, 460, 6th ed.

defective development of the esophagus and with atresia of the rectum have been observed. Drennan and Clark⁹ state that but one point of actual closure usually exists, but that, in addition, one or more points of stenosis may be found.

Productive fetal peritonitis and enteritis, thrombosis of the mesenteric vessels, anomalies in the development and distribution of the blood vessels, volvulus, intussusception and anomalies of the yolk stalk have been given as the possible causes. Rowland¹⁰ reported one case and mentioned four others which, at operation, showed a complete twist of the mesentery of the small intestine. He also says that inspissated meconium may cause complete obstruction, and that this may be fatal or may be spontaneously relieved. He refers to a fatal case. Holt¹¹ believes that congenital syphilis may be an etiologic factor. As Cordes says: "The aforementioned causes certainly do not explain the greater number of the cases and other factors, probably developmental defects, coexist."

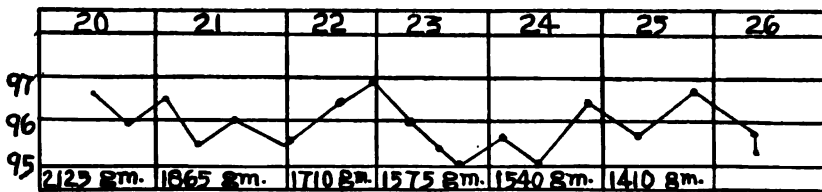


Fig. 1.—Temperature curve and weight variations.

Kreuter (quoted by Kaufmann⁸) asserts that there is absence or imperfect development of the lumen of the intestinal canal at a certain time in the development of the embryo (thirty to sixty days). At first the intestine is hollow, but as a result of hyperplasia of the lining epithelium, temporary closure results, which, in the normal fetus, later reopens. Failure to reopen gives various types of atresia or stenosis. Schridde denies this, having never found epithelial atresias. Forssner,¹² however, supports Kreuter's hypothesis, stating that just above the narrow point, as a result of swallowing amniotic fluid, there is enormous dilatation of that portion of the intestine with an accompanying hypertrophy of the muscularis. Purulent infiltration of the intestine and perforation may result. The lower segment collapses, the wall atrophies and the lumen may be totally obliterated.

9. Drennan and Clark: *AM. JOUR. DIS. CHILD.*, 1915, **10**, 360.

10. Rowland, V. C.: *AM. JOUR. DIS. CHILD.*, 1915, **9**, 455.

11. Holt, L. E.: *Diseases of Infancy and Childhood*, 1916.

12. Forssner, H.: *Hygiea*, Stockholm, 1912, **74**, 1168; *Ibid.*, *Arch. f. klin. Chir.*, Berl., 1912, p. 477; *Ibid.*, *Zentralbl. f. Chir.*, Leipzig, 1913, **40**, 193.

Thorel's¹³ case had seven points of atresia. He described the epithelial proliferation as the cause in his case and believed that it is the probable cause in most cases, unless there is rotation of the intestine, which, however, is very rare.

Quain¹⁴ and Bailey and Miller¹⁵ agree with Kreuter's theory as to the mode of origin of this condition, and considering the embryologic

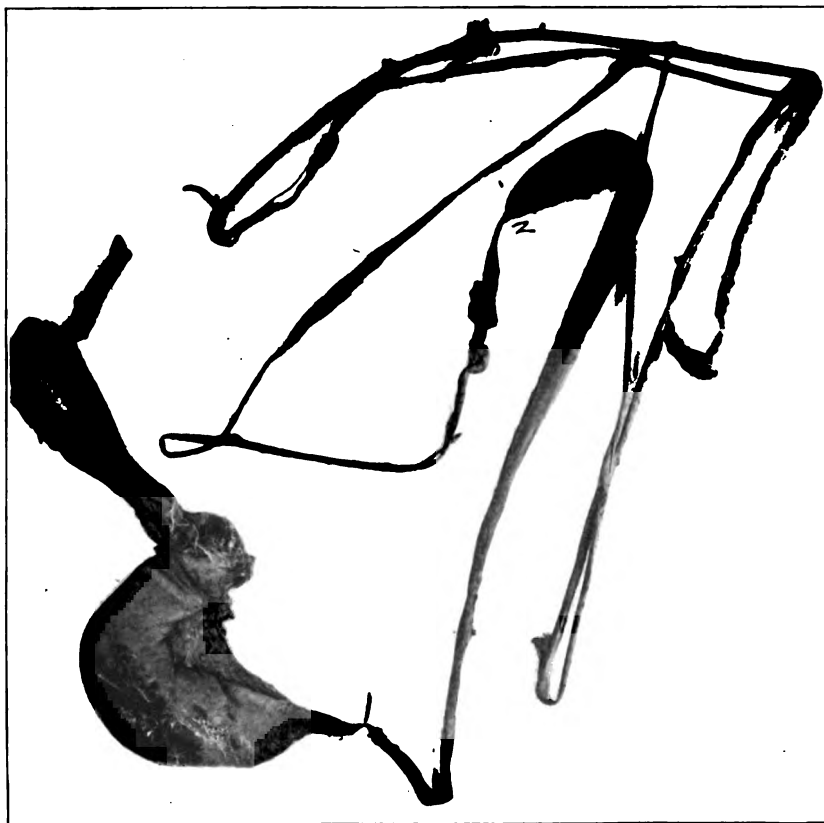


Fig. 2.—Large and small intestine showing strictures at 1 and 2

development of the intestine, it is evident that this process will account for a considerable number, if not the majority, of the cases of congenital intestinal obstruction.

The following symptoms, which were not recorded in our case, are of sufficient importance to remember in arriving at a diagnosis.

13. Thorel, F.: *München. med. Wchnschr.*, 1899, **46**, 1202.

14. Quain: *System of Anatomy, Embryology*, **1**, Part 1, Ed. 10, 1896, p. 99.

15. Bailey and Miller: *Textbook of Embryology*, Ed. 1, 1910, p. 358.

Schwalbe¹⁶ noted that in high stenosis the abdomen is retracted and in low stenosis the abdomen protrudes.

Pfaundler and Schlossmann¹⁷ mention the following symptoms: Abdominal pain, obstinate constipation, deficient flatus, uncontrollable vomiting (at first food, later mucus, bile, blood and "kot"), meteorism, purposeless visible peristalsis, intestinal spasticity, tumor (Nothnagel's phenomenon) and finally collapse. They divide them into obstructions occurring in the small intestine and those in the colon and make a differential diagnosis according to the following table:

	Obstruction in Small Intestine	Obstruction in Colon (Lower Half)
Meteorism.....	Changeable, moderate and only epigastric lower and side parts of abdomen sunken.	Constant, strong and universal; "Kotwülste" palpable
Vomiting.....	None, or occasionally fecal	Fecal
Urine.....	Indicanuria, oliguria	No indicanuria; no oliguria
Collapse.....	Very severe	Moderate

REPORT OF CASE

The following case came to necropsy in Bellevue Hospital, Sept. 26, 1917.

History.—A girl, the second of twins, was born Sept. 20, 1917, of a healthy mother (Di R. M-3, service of Dr. J. C. Edgar, visiting obstetrician to Bellevue Hospital, to whom I am indebted for permission to abstract the clinical record). Family history negative; Wassermann on mother negative. At birth the patient was bleeding quite profusely from the nose and mouth. No other abnormality was noted. Shortly after birth the infant passed a small amount of meconium. The bleeding continued, although to a less extent, through the day, and at 8:30 p. m., 10 c.c. of horse serum were given intramuscularly. Thereafter bleeding diminished very materially. The total amount of blood lost during this time was estimated at about 1½ ounces.

September 21. Immediately after the administration of a small amount of water the infant vomited a brownish fluid. When given the breast at 3 p. m., the child nursed exceedingly well, but a few minutes later vomited a thick brown residue. Blood oozed from nose and mouth throughout the day. At 5 p. m. 10 c.c. of the mother's blood was given, with but slight improvement in the child's bleeding. There was no bowel movement and the urine was scanty.

September 22. One ounce of saline was given into the rectum but was not retained; large amounts of mucus were expelled. Oozing of blood from mouth and nose occurred during the entire day, but stopped during the night. The child continued to vomit dark brown material after each feeding. There was no bowel movement.

September 23. Vomiting continued after each feeding. Vomitus this day was thick yellowish streaked with brown. Three ounces of olive oil given per rectum was not retained but was immediately expelled together with mucus. Bleeding continued. Pulse rapid (120), weak.

16. Schwalbe, E.: *Morphologie der Missbildungen des Menschen und der Tiere*. Ed. 1, 1909, 3, 58.

17. Pfaundler and Schlossmann: *Handb. der Kinderh.*, 1, Part 1, Ed. 1, 1906, p. 72.

September 24. Eight drops of castor oil and saline enema given but without effect. Other symptoms as heretofore. Wrapped in cotton; kept warm.

September 25. Symptoms as before; bleeding continued; urine continued scanty.

September 26. Died at 1:55 p. m., following a profuse vomiting of yellowish material containing a large amount of blood.

Clinical Diagnosis.—Intestinal obstruction (congenital); hemorrhagic disease of the new-born.

Necropsy.—The body was that of an emaciated, white female infant, weighing 1,325 gm. and measuring 42 cm. in length. Rigor mortis was absent, and there



Fig. 3.—Microscopic section taken at 1 in Figure 2.

was a slight postmortem diffusion over the back. The entire skin was markedly icteric and there were ecchymotic areas over the lower extremities, on the back and the chest. The scalp was clean and covered by a fair amount of fine, long, black hair. Both fontanels were open and depressed. The pupils were equal and in middilatation; the sclerae were markedly icteric; conjunctivae free of petechiae and discharge. The nose and ears externally were negative. The lips were pale; the mucous membrane of the mouth was smooth. The tongue was dry, not fissured and there were no ulcerations present. The superficial lymph nodes were palpable only in the groin. The chest was symmetrical. The outlet of the thorax was acute. The abdomen was scaphoid. The external genitalia were normal. The extremities were normal.

The abdomen was free of fluid. The umbilical vein and both hypogastric arteries were patent. The greater portion of the large and small intestines was collapsed. There were numerous subperitoneal hemorrhages in the parietal and visceral peritoneum covering the intestines, the stomach and the liver. The mesenteric and retroperitoneal lymph nodes were not enlarged. The liver extended about 15 mm. below the costal margin. The diaphragm reached the fourth space on both sides. The stomach and about 9 cm. of the duodenum were distended with a dark semi-fluid material; and there was an apparently complete stricture of the duodenum, following which the jejunum, for a distance of about 20 cm., contained similar semi-fluid residue, and at this point there was another apparently complete stricture (Fig. 2). It was impossible to force the

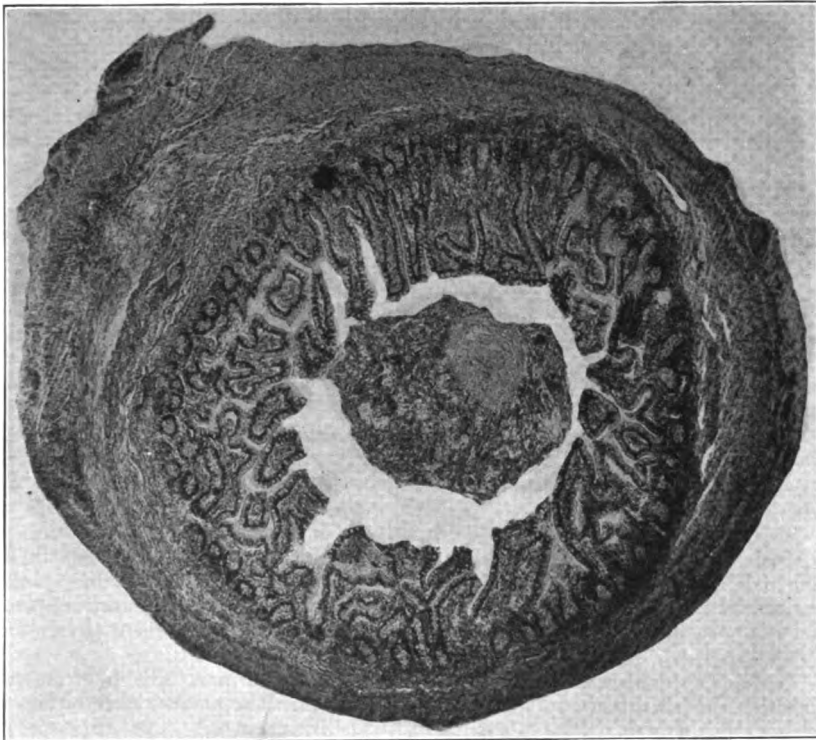


Fig. 4.—Microscopic section taken at 2 in Figure 2

intestinal contents through the stricture. The organs were in their proper position. There was no rotation of any portion of the intestine. The remainder of both the small and large intestines was totally collapsed. The appendix was small and lay free over the pelvic brim. A probe could be inserted into the rectum for a distance of $1\frac{1}{4}$ inches.

The right pleural cavity contained about 0.5 c.c. of a dark, hemorrhagic fluid. There were no adhesions. Over both the visceral and parietal pleurae of both lungs there were a number of large hemorrhages scattered in irregular fashion and presenting no definite demarcation. The pleural surfaces were smooth and of a bright red color, except where the irregular darkened hemorrhagic areas were found. The lung on section cut smoothly, presenting an irregularly reddish, mottled, crepitant surface, from which but little fluid could be expressed. The

bronchi were normal and were free of fluid. The peribronchial and mediastinal lymph nodes were not enlarged. The branches of the pulmonary artery were normal.

Heart: The precordial area was normal. The pericardial sac contained a small amount of dark hemorrhagic fluid and there were also some hemorrhagic areas on the epicardium. There were no petechiae present. The heart was of normal size, dark red in color. The epicardium was smooth. There were no subendocardial hemorrhages present. The heart chambers contained a moderate amount of dark red fluid blood. The valves were normal and apparently competent. The fossa ovalis was small, the foramen was patent. The myocardium was smooth and, on section, of a dark red color. The coronary vessels, as far as examined, were normal. The aorta and pulmonary artery were both smooth and elastic and without intimal change. The ductus arteriosus was closed.

The thymus was of normal size and weighed about 10 gm. On section it presented pale pink, glandular tissue.

Liver: This was of normal size. The capsule was not thickened. It was of a dark red color. On section it presented a firm, dark red surface from which a good deal of blood exuded. The vessels and duct were patent. The latter was considerably distended with bile. The gallbladder wall was smooth. The organ contained a small amount of thick, yellowish green bile.

Spleen: This organ was of normal size; it was firm. The capsule was not thickened. On section it presented a dark red surface in which the malpighian corpuscles were not prominent.

Pancreas: This was small, of normal consistency and the section was normal.

Kidneys: The kidneys were small and embedded in but little fat. They were considerably lobulated. The capsule stripped readily, leaving a pale reddish surface. On section there was distinct demarcation between cortex and medulla. The pyramids appeared a little swollen and contained well defined, radiating, orange-colored uric acid infarcts. The pelvis of the right kidney contained a few small, hemorrhagic areas. The ureters were normal.

The bladder was contracted and contained a small amount of urine. The wall was smooth and without lesion in the gross.

The adrenals were of normal size and on section, normal. There were no hemorrhages seen.

The uterus, tubes and ovaries were normal in the gross.

Organs of the neck and throat: The tonsils were small and pale pink in color. The trachea was normal in appearance. The esophagus to within about 1½ cm. of the cardia was normal. The remainder of the gastro-intestinal tract was not opened, but preserved in formaldehyd solution for subsequent sectioning. The thyroid was small; on section normal.

Head: The scalp was readily stripped from the calvarium. The anterior and posterior fontanels were both patent and depressed. The sutures overrode to a considerable degree. The calvarium was readily removed. The dura mater was normal. There was a considerable amount of pial edema present. The brain was soft. Section of the cerebral hemispheres was normal. The lateral ventricles were without fluid. There were no hemorrhages anywhere. The floor of the fourth ventricle had a decided yellowish tinge; otherwise it appeared normal. The examination of the middle ears and the sinuses accessory to the nose was negative.

Examination of the lower extremity of the right femur was negative.

Anatomic Diagnosis.—Congenital intestinal obstruction; hemorrhagic disease of the new-born (involving skin and serous surfaces); icterus neonatorum (obstructive jaundice?); uric acid infarction of kidney; pial edema, marked; patent umbilical vein, hypogastric arteries and foramen ovale.

Microscopic examination of the tissues and organs showed nothing remarkable.

Microscopic sections taken from the intestine at points indicated in the photographs (Figs. 3 and 4) show complete destruction of the lumen of the duodenum (1) and replacement by fibrous tissue in which there are a number of

blood vessels. There is no suggestion of a lumen. Section (2) made through the second point of constriction shows a lumen which is markedly diminished in caliber and occupied by a small blood clot.

The anatomic details of the foregoing case are in close agreement with those of three cases recorded by Ducros,¹⁸ who found complete atresia of the duodenum-jejunum junction due to the presence of a fibrous mass replacing the lumen.

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METHODS USED IN A CLASS FOR UNDERNOURISHED CHILDREN *

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During the past few years attention has been repeatedly called to the fact that a large number of children in this country are undernourished. That this is true has been shown by the reports of school inspectors and by several different surveys made by other agencies. These have been summarized recently by Baker¹ and by the report of the Public Health Committee of the New York Academy of Medicine.² The exact amount of this malnutrition is estimated differently by various observers, and this is partly due to the fact that there is no accurate or standard scale by which to measure the nutrition of the child. In some of the surveys no weights were taken, but the nutrition was merely left to the judgment of the observer. Nevertheless, there is no doubt that the amount of malnutrition is not inconsiderable, and that it promises to mount to an alarming degree unless its existence is recognized and measures are taken to combat it. The various estimates range from 10 to 30 per cent. of distinctly undernourished children in the public schools of New York City. Even at the lowest figure this means 100,000 children.

Any physician who has worked in a children's outpatient department will readily grant that this problem has not been recognized or met in the past. The undernourished child who has no interesting signs of organic disease has had scant attention. He has been put aside with a diagnosis of "anemia" or "malnutrition" or perhaps has been called "pretuberculous." He may have been given an iron tonic or cod liver oil at his first visit, but in the vast majority of cases no effort has been made to ascertain the underlying reason for his undernourished condition, or to induce him to return for subsequent observation or treatment.

* Submitted for publication April 10, 1918.

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1. Baker, S. J.: New York Med. Jour., Feb. 16, 1918, p. 289.

2. Report of the Public Health Committee, Med. Rec., New York, Feb. 23, 1918, p. 311.

Nov. 1, 1916, a Nutrition Class was started in the Outpatient Department of Bellevue Hospital as an experiment to determine how much could be done to improve the nutrition of undernourished children when handled in large numbers. It is well known that much can be done for individual children who are under-weight if their lives can be properly regulated, and that groups of children can be made to gain at much more than the average rate in institutions, camps and so forth. It is a comparatively easy matter to make any group of children gain rapidly when their diet and habits can be completely controlled. But controlled groups in institutions are of necessity small, and the children who are made to gain while under control are very apt to lose much of the accumulated weight when they return to their homes and to the former insufficient diet and unhygienic mode of life. Some plan must be devised by which the malnutrition problem can be attacked on a large scale, and which will strike at the very root of the trouble, that is, the daily life of the child in his own home.

The class system offers one of the ways in which this may be done. It has long been used for tuberculosis in adults and children and has given admirable results. The class plan as applied to undernourished children, to patients with heart disease, and to other groups, has nothing new in principle. Each group of patients studied has its own problems, however, and new methods must be worked out for each.

The nutrition class was planned as one of a number of classes for the treatment and study of special conditions at the time of the reorganization of the Children's Medical Division. The Health Department loaned one of its school nurses through the association for the Improvement of the Condition of the Poor, and this nurse has acted as social worker for the class since its beginning. The Association for the Improvement of the Condition of the Poor through its Bureau of Child Welfare, also rendered assistance in compiling and studying the statistics obtained during the first months of the work.

The methods which are used in this class have been worked out in the children's tuberculosis class and other classes at the Vanderbilt Clinic, to which have been added valuable methods obtained from the papers of Emerson³ of Boston and from other sources. To Emerson must be given great credit, since he has been the pioneer in calling attention to the existence of large numbers of delicate children, and also to the value of the class method in treating them. The conditions of the work in the Bellevue Hospital Class under which one physician is compelled to take care of from forty to sixty children in an afternoon have necessitated the adoption of a great many short-cuts and time-

3. Emerson, W. R. P.: *Boston Med. and Surg. Jour.*, 1910, **163**, 326; *Ibid.*, *Pediatrics*, 1910, **22**, No. 9.

saving methods which are absolutely essential when large numbers must be handled by one man. It was planned originally to have several physicians at work in the class, but the entrance of this country into the war so reduced the staff that the work has been done by one or two men.⁴ Volunteer women workers have assisted much in the conduct of the class. Without their aid it would be impossible to handle the large numbers who have attended.

The patients in the nutrition class have come from several sources. The markedly undernourished children who apply to the outpatient department for treatment for any condition whatever, and also the undernourished children discharged from the wards, are referred to the nutrition class. The school nurses from the neighboring schools have sent a large number of children and they have also come from agencies all over the city.

Every child who has applied for admission to the class has been accepted if he has been 5 pounds or more *underweight for his age*. A large number of patients have been referred who were actually overweight, simply because they looked a little pale or thin. These children have all been examined and advised, but have not been enrolled in the class.

There have been enrolled as members of the class.....	290 children
Discharged on account of refusal to attend.....	77
Moved away	14
Not found	6
Transferred to tuberculosis class.....	3
Working	2
	— 102 children
Remaining regular in attendance.....	188 children

The children return at varying intervals, from once a week to once a month. The average attendance is from thirty-five to forty, and since the class is held twice a week about one third of the children are seen each week. The follow up work has all been done by one social worker, and it is manifestly impossible properly to follow every case as fully as is desirable. At least one visit has been made to each home, and the subsequent visits have been made on families where the need seemed greatest. A follow up card index is used, and postals are sent to ask mothers to return, when their visits are irregular. The postal is followed by a visit if it brings no response.

4. Dr. H. L. Bibby, who is now in France, and Dr. L. C. Schroeder have assisted during part of the past year.

We have made it a rule that the parent or some adult member of the family must come to the class for the first few visits so that advice and instructions can be given to a responsible person. After the first visit most of the children have come alone, because it does not seem fair to exclude a child simply because his mother is unable to come every week. It would be much better, of course, to have the parents attend regularly, and many of them have done so from choice, but so many of the mothers are kept at home by the other children, by housework or by actual employment, that the percentage of attendance of mothers has to be necessarily quite low. In this regard, as in many others, we have deliberately fitted the plan of the class to the conditions which exist and have not laid down any hard and fast rule which would exclude many children who need treatment. The children whose parents have attended regularly have naturally done better than those who have come alone, as the advice given to a child who comes alone may or may not be transmitted to the parent in the form in which it is given. It is also perfectly futile to tell a child he must not drink coffee and must take milk and cereal when his answer is that his mother gives him only coffee and buns, but in many instances by repeatedly urging the child to ask his mother for the right food we have attained the end for which we have aimed, even though the mother was not able to come to the class.

The Routine.—Each child has had a fairly complete history on admission to the class on the printed history form used in the department. This includes a careful family history, past history, and analysis of the child's daily habits: time of going to bed, getting up, sleep, open window at night, amount of time outdoors, number of hours in school, bowel habits, quality and quantity of food taken at each meal and between meals, the amount of tea, coffee, beer, candy, etc. The present history is added, including the source from which the patient is sent, and the reason for which the child is admitted to the class, and any symptoms which he may present at the time. A complete physical examination is made of every child, including his weight and height. A von Pirquet test is made at the first or subsequent visit. The blood and urine are examined when possible. The social worker gets the social service facts either at the first visit, or at her first visit to the patient's home, and these facts are entered on the medical history by means of a rubber stamp. Everything of importance from the physical and economic standpoints is thus noted on the medical history. It has too long been the custom to have social service data carefully

The rubber stamp used for the social data bears the following:

Living, Health, Alcoholic, Working, Occupation, Wages,

Family Income

**{ Intelligent?
Responsive?
Clean?**

Number Working

**Number
Dark**

Sanitary Condition

ADVICE AND ASSISTANCE

HOME, Improved, Unimproved

PATIENT	T.	P.	R.
---------	----	----	----

TREATMENT AND ADVICE

At the first visit an attempt is made to pick out the important elements which bear on the child's malnutrition. A short talk is given to each mother and child on the errors of hygiene of which that child is guilty. The child's daily life is gone over carefully; the importance of early hours, sufficient sleep, cleanliness, regular bowel movement, eating slowly, and above all of eating the proper kind and sufficient amount of food, is emphasized as strongly as possible. If there are any decayed teeth the child is referred to the dentist, or taken to him by the nurse. If the tonsils or adenoids are giving symptoms or if they are much enlarged, operation is advised provided the child's

general condition warrants it. When the nutrition and general condition are extremely bad it is often better to wait a few months and try to make the child more fit for an operation. There is nearly always a loss of weight after a tonsillectomy and if a child is operated on when he is in very bad condition the recovery of the additional loss in weight is very slow. It is also important to keep the child in bed for at least five days after tonsillectomy, or the loss in weight may be excessive.

CHILDREN'S MEDICAL HYGIENE

BELLEVUE HOSPITAL

OUT PATIENT DEPARTMENT

PROPER FOOD FOR CHILDREN OF SCHOOL AGE

BREAKFAST				CHEAPER	MORE EXPENSIVE	MOST EXPENSIVE
1. CEREAL	2 to 6 tablespoons	Coat 2 hours eight hours, in double boiler, or before water		Bulk Cereals Oatmeal, Cornmeal, Hominy, Rice Flakes.	Cornels in packages Wheatons, Malt Branched Food, Cream of Wheat, Pampana's	Strawbed Wheat, Flax, Corn Flakes, Puffed Rice
2. MILK or CUCOA	1 cup 1 cup	1 teaspoonful to a cup (not milk, but water)		(Milk gives the most food for the money even when very high priced)		
3. BREAD AND BUTTER	1 to 2 slices	(made or toasted)		Whole Wheat, Graham or Corn Bread	White Bread	Rolls
4. EGG		(not boiled or poached or scrambled with milk)		Not Margarine or Oleomargarine are just as something as Butter which costs about twice as much		
5. FRUIT		Coat 2-3 hours without sugar. Soak over night if very dry		Cooked Apples, Stewed Prunes Stewed Dried Peaches Stewed Dried Apples	Orange or Grapefruit	
DINNER						
1. SOUP	1 bowl			Vegetable soup - made from Peas, Split Peas, Beans, Lentils (from lot given above)		Meat Soups if given should be thickened with rice or barley
or CEREAL	2 to 4 tablespoons					
or EGG		(not boiled or poached or scrambled with milk)				
2. MILK	1 to 2 cups					
3. BREAD AND BUTTER	1 to 2 slices	(made or toasted)		Whole Wheat, Graham or Corn	White Bread	
4. COOKED FRUIT	2 to 3 tablespoons			Apple Sauce, Baked or Stewed - Apples, Stewed Prunes, Stewed Dried Peaches	Stewed Dried Apples, Baked Apples	Fresh fruit, peaches, pears, oranges
SUPPER						
1. MEAT	a small piece about 2 ounces	Stew, boil, roast or broil Do Not Fry!		Lamb Steak, Beef Steak, Pork, Lard, Friedsteak, Hashbrown, French Hashbrown	Chopped Beef Chicken	Roast Beef, Broiledsteak, Roast Lamb, Lamb Chop
or VEGETABLE SOUP	1 bowl			made from Peas, Split Peas, Beans, Lentils or any of fresh vegetables		Beef or Meat Soup with rice or barley
2. VEGETABLES				Squash, Chard, Beet Tops, Greens, Carrots, Beets, Boiled Onions Lima Beans, (cook 3 hours)	Peas, String Beans, Squash Stewed Cabbage, Knob Cabbage	Cauliflower Oyster Plant Potatoes
Fresh Vegetables	2 to 4 tablespoons	Put over small amount of boiling salted water until tender, drain off all the water.				
and						
Starchy Vegetables	2 tablespoons	boiled, baked, mashed Do Not Fry!		Potatoes, Sweet Potatoes, Rice, Hominy, Spaghetti, Macaroni		
3. BREAD AND BUTTER	1 to 2 slices	(made or toasted)		Whole Wheat, Graham or Corn Bread	White Bread	
4. DESSERT	1 to 2 tablespoons			Rice, Tapioca or Bread Pudding Custard or Corned puddings Cooked fruit, (from lot given above)	Junket, Custard Custard Pudding	Custards, Ice Cream

DO NOT GIVE

1. TEA, COFFEE, soda water, beer, wine, whiskey, cider.
2. Fried food of any kind.
3. Pork, veal, kidneys, greasy stews, gravy made from drippings or grease.
4. Corn, cabbage, cucumbers.
5. Fresh breads, buns, cake, pie, fried cakes, rich puddings.
6. Nuts, raisins, berries, cherries.
7. Candy, jelly, sweet preserves.
8. Too much milk - one quart a day at most is enough for any child.

Every child needs at least one pint a day.

RULES FOR EATING.

Give no food between meals unless ordered by doctor. If a child is very hungry after meals give him a piece of bread and butter, NOT cake or fruit. Make every child eat slowly and chew his food well and not wash it down with water or milk. Allow child to drink only one glass of water with each meal. Urge children to drink water between meals but not at bedtime. Make every child wash his face and hands before meals.

DRINK FOOD WARM and WELL COOKED on clean dishes and a clean table. KEEP FUR AWAY FROM FOOD. One fly can give typhoid or summer complaint. BUY ONLY BOTTLED MILK, and ALWAYS KEEP ON THE ICE.

Fig. 1.—Reproduction of diet list (reduced).

A printed slip with directions as to the general care of the child and a diet list (Fig. 1) are given to every mother, and these are explained carefully in an effort to prevent her from thinking them unimportant pieces of paper. The diet list has been rewritten several times in collaboration with the director and the attending physicians of the Children's Medical Division, and with the dietitian of the Association for Improving the Condition of the Poor. The first lists used were simply an ideal diet for a child, but it was found that the expensive foods which occupied the most prominent place on the lists dis-

couraged the mothers from trying to pick out a dietary within their means. In the revised lists the various foods are sorted according to their relative cheapness. In the first column (Fig. 1) appear the articles of food to be taken at each meal; in the second the amounts of each; the third column gives some simple cooking directions. The various articles of food are then arranged in order of their cheapness and importance. Thus, it is seen that milk is put in the fourth column, not because it is a cheap food, but because it really gives more food for the money than many apparently cheaper foods. White bread is put among the more expensive foods because it has less of the desirable elements than whole wheat and graham, although it costs about the same. Since this diet list has been in use it has been found that the parents respond to it much more readily than to the earlier one.

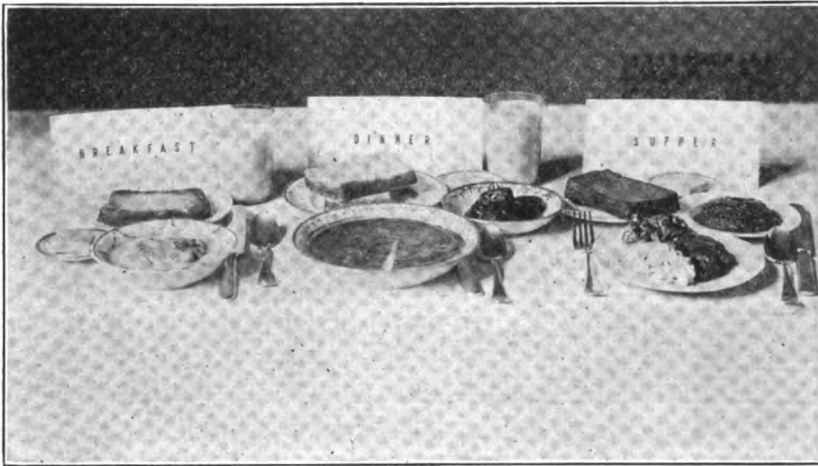


Fig. 2.—Exhibit of artificial foods, showing the way in which three meals are placed on the table. This arrangement is varied each day.

At the first visit the attention of the mother and child is called to the *food exhibit*, as an aid to impressing on their minds the elements of a proper diet. This exhibit differs in important respects from those in common use. Most of these have been composed of quantities of food which represent hundred calory portions, or other units, and merely show the relative value of the various foods from the energy standpoint. They do not show the relative desirability of foods from other than this point of view. For example, a plate containing three or four large tablespoonfuls of vegetable shows that vegetables are relatively poor in energy-yielding substances, but there is danger that an ignorant mother may think a child should eat four or five large table-spoons of a green vegetable and only a comparatively small quantity of cereals or other food high in caloric value.

The food exhibit which we use is based on the day's total ration. Three meals are laid out each day: breakfast, dinner and supper. The mother and the child can both then see at a glance the total amount of food needed in the day, and also the exact composition of each meal. These meals are laid out as if ready to serve, with dishes, knife, fork and spoon, and each meal is properly labeled (Fig. 2). The breakfast usually consists of a dish of cereal with milk or a cup of cocoa, two slices of bread and a pat of butter, and sometimes an egg or fruit. The midday meal is varied according to the age of the child, and is also changed from time to time as it is placed on the table. A dish of thick vegetable puree, a glass of milk, two slices of bread, a pat of butter and a baked apple form the average midday meal. The main part of the evening meal is shown on a plate containing one kind of meat or fish, potato, macaroni or rice, a green vegetable, two slices of bread, a pat of butter, a glass of water and some stewed fruit.⁵ The exhibit is rearranged every day. There are several plates which can be interchanged so as to give variety to the meals. When the exhibit is being explained to a mother, these are changed rapidly so as to impress on her the fact that the diet is not too hard and fast, but at all times the table presents to her eyes a picture of three meals which are well balanced, well cooked, well served and at the same time not beyond the means of the average family.

This exhibit has great educational value. The visual impression made on the mother and child adds tremendously to the significance of the printed list of foods given out on the diet list. In the case of people who do not speak English this is practically the only way in which they can be reached. A list of the units used in the exhibit is as follows:

1 dish of oatmeal with milk	1 plate with a poached egg on toast
1 dish of cornmeal with milk	1 plate thick vegetable soup
1 dish of wheatena with milk	1 plate puree of peas
3 plates with two slices bread on each	1 plate Irish stew
1 plate with one slice brown bread	1 plate with chop, baked potato, spinach
1 plate with two or three pieces of Zwieback	1 plate with fish (boiled halibut), rice, string beans
3 butter dishes with one pat of butter	1 plate with meat ball, macaroni and carrots
2 glasses of milk (8 ounces)	1 baked apple
1 cup cocoa	1 plate apple sauce
1 orange	1 dish prunes
1 cookie	

5. The exhibit was made up in large part by Yaeger & Co., 1495 Third Avenue, to which were added foods obtained from other sources. The imitations are so real in appearance that nearly every one is deceived at first glance. They are durable and not expensive. The food exhibit is also of great value in teaching students. The hearty evening meal may meet with some objections. This has been advised for schoolchildren because of the short noon hour and because it saves the mother from cooking two dinners, since the father must have his main meal at night. For younger children the hearty meal is at noon.

It is very simple to calculate the food value of the day's total from the portions comprising the various meals. Nearly all of the foods are arranged in portions approximating 100 calories each and the total calories a day can be rapidly reckoned with a reasonable degree of accuracy.

Besides the three-meal food exhibit we also use a certain number of hundred calory portions to compare foods of low and high energy content. Thus, a half ounce of olive oil, 5 ounces of milk and a quart of soup placed in a row make an impression which is of no small value. In the class of society with which we have to deal, however, it is futile to attempt to spend much time in educating ignorant mothers as to accurate hundred calory portions. It seems to me that the food value is the thing which the physician should constantly carry in his own mind in prescribing diets, but the less the patient is confused by extra and somewhat artificial factors, the better. Among the better classes, with people of intelligence, the study of food values is useful, and even children can be easily taught to count the calories in their meals; but when it takes every persuasive power which the physician has at his command to induce a mother to cook cereal, and to give the child cereal and milk instead of coffee and a roll, it is absurd to distract the mother with the discussion of the amount of a hundred calory portion. If children can be taught to take a bowl of cereal and a portion of vegetable and cooked fruit, the battle is half won.

Class talks are given frequently to groups of mothers for the purpose of saving time, and the effort is made to include in these the mothers who are newest in the class. From time to time talks or lectures are given to the entire class, and the whole matter of the daily régime and the diet from every possible angle gone over again and again in the hope that reiteration will drive home the things we are trying to teach. Wall charts have been very useful, one showing what makes a child gain, and another what makes a child lose. (Figs. 3 and 4.) A great many of the children have memorized these charts and recite them off in chorus like children in school.

Return Visits.—At the first visit the children and mothers are urged to return once a week. On account of the large number of patients under observation this interval has been increased to two or three weeks as soon as the child has begun to do well, but if the gain stops he is again asked to come each week. At the return visit the children are seen in groups, but each child is given individual attention. Twenty or thirty children stand around the physician's desk while he talks to each in turn, reads the notes made by the social worker or volunteer assistants, and the home record made by the child, and makes additional notes on the patient's progress. A rubber stamp is used for

noting the principal facts of the child's hygiene and diet, and this is filled in whenever a child fails to gain a satisfactory amount.⁶ This insures more or less parallel series of records on the return visits.

WHAT MAKES A CHILD LOSE

FOOD - TOO LITTLE
 WRONG KIND **TEA COFFEE**
 FRIED FOOD
EATING TOO FAST
SLEEPING TOO LITTLE
RESTING TOO LITTLE
STALE AIR - CLOSED WINDOWS
CONSTIPATION OR IRREGULAR BOWELS
DIRTY HANDS FACE BODY CLOTHES
BAD TEETH

Figure 3

WHAT MAKES A CHILD GAIN

FOOD - RIGHT AMOUNT
 RIGHT KIND
EATING SLOWLY
SLEEPING ENOUGH - 7 TO 7
RESTING 1 HOUR AFTER DINNER
FRESH AIR OPEN WINDOWS
BOWEL MOVEMENT AFTER BREAKFAST
CLEANLINESS
GOOD TEETH

Figure 4

Figs. 3 and 4.—Large wall charts which are used as texts on which to base class talks. Charts of this kind may be easily made by the use of gummed letters.

The questions can be asked and the blanks filled out by a volunteer lay worker after comparatively little training. By this group method every child hears the correction of the mistakes of every other child

6. Breakfast
 Dinner
 Supper
 Bed at Up at

Bowels move at
 School hours
 Out doors
 Reason for loss

and each child gets a maximum number of impressions as to the desirability of regular habits and diet. The children are asked to correct each others' faults also. It is most interesting to see how well some of the children pick out the reasons for the failure of a given child to gain.

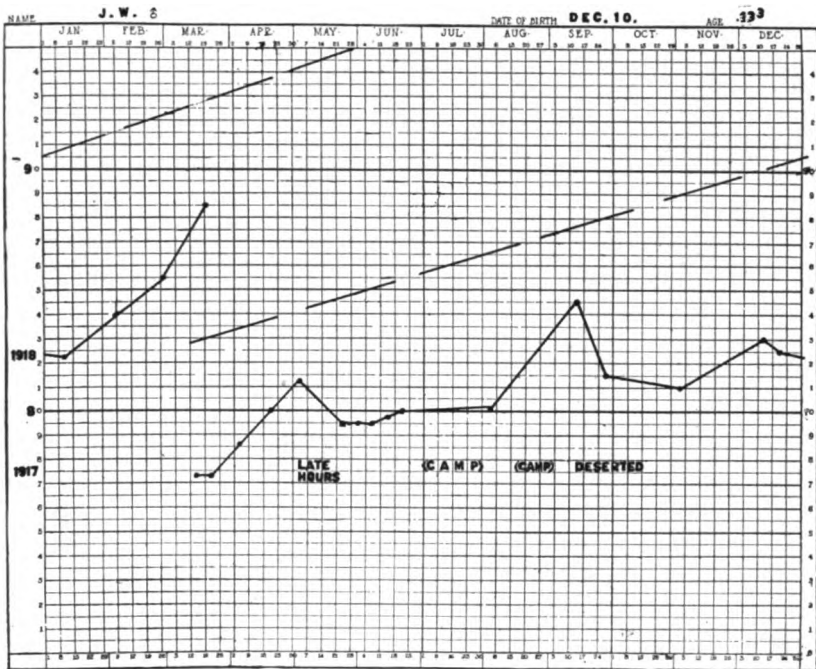


Fig. 5.—J. W., boy, aged 13 years 3 months. This boy was of average height ($56\frac{1}{2}$ inches) and nearly 6 pounds under weight. When he first came he had been taking the usual insufficient and improper diet, his bowels were irregular, he rarely went to bed before 10 or 11. Teeth, six cavities; von Pirquet positive. He responded to the suggestions given at the class and gained well at first, but after a time became "weary of well doing" and began to sit up late again, with the loss to be expected. In the first four weeks in July he was at a camp in the country but made no gain. Later he spent two weeks at another camp and gained $4\frac{1}{2}$ pounds. In late September the father deserted the family. This affected the boy greatly, he slept little and "grieved for his father." The family income also dropped, but after a few months the mother began to earn enough to buy more food, and the boy rallied from his grief. He has gained 11 pounds in a year, while the expected gain is 10 pounds. The broken line shows the average weight for his age.

The children who have gained well are praised and held up as examples to be followed by the class. If they have gained regularly for several weeks they are told to come less often. Children who have not gained satisfactorily or who have lost are turned over to the social worker or volunteer for careful questioning. The temperature

is taken at each visit in all cases in which a child has failed to gain under apparently good care. After the careful questioning of the child, a second physical examination is made in children who are doing badly, and much of the time is spent in trying to find a correct cause of failure to gain.

Some children are stimulated greatly by pasting a gold star on the chart when the gain has been large. This seems almost too

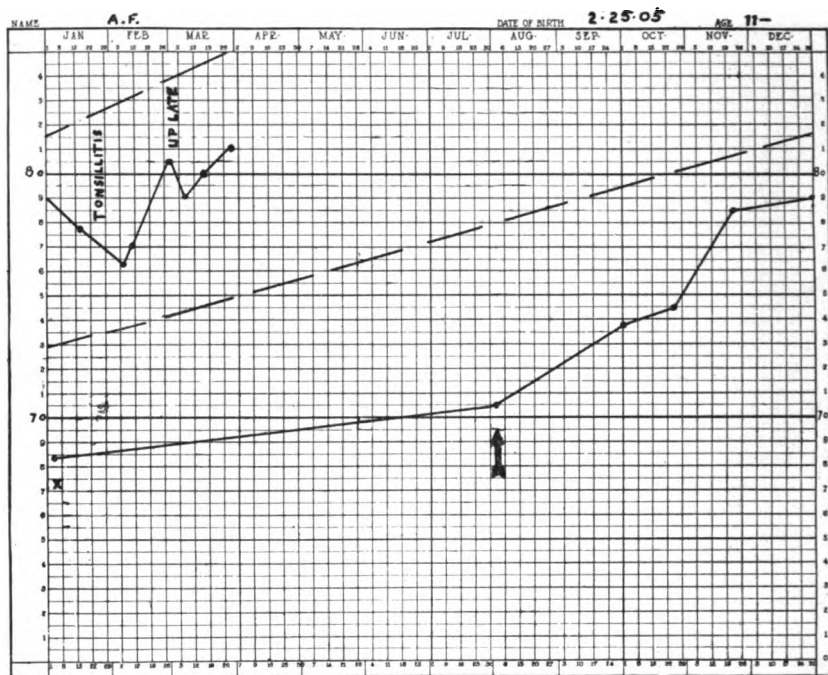


Fig. 6.—A. F., girl, admitted to general clinic for a cold at X. Admitted to nutrition class at arrow. Note difference in rate of gain thereafter. Loss caused by tonsillitis followed by quick recovery. Sat up late two or three nights and lost $1\frac{1}{2}$ pounds, but regained this in the next few weeks when she went to bed early.

On Admission to General Clinic		15 Months Later	
Age.....	11 years 10 months	Age	13 years 1 month
Weight	67 3/4 lb. Average 73 lb.	Weight	81 lb. Average 84 lb.
Height	56 1/2 in. Average 54 1/2 in.	Height	57 in. Average 57 in.
Average weight for height....	81 lb.	Average weight for height	84 lb.

Broken line is average weight for age.

trivial to be of consequence, but the gold star has certainly encouraged a great many children to keep on trying. Prizes have even more value. A monthly prize is given for the greatest gain for each boy or girl. The children are asked to pick out their own prizes to a certain extent; that is, the children are asked to suggest prizes which they

would think worth trying for. Pencil boxes, boy scout suits, skates, toys and dolls are not very expensive and are effective.

Children have not been sent away from home unless it has been proved by a thorough test that they cannot be made to do well in their homes. If the test at home is a failure, a month or two away in a good institution or camp often starts a gain and establishes a habit of growth which continues after the child's return. Short stays in fresh

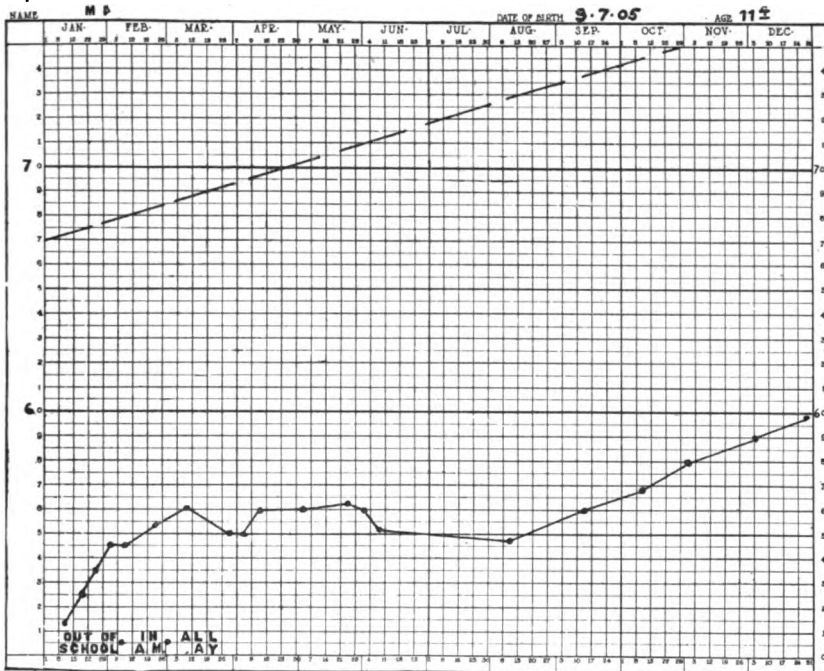


Fig. 7.—M. P., girl, aged 11 years 4 months, shows the effect of school attendance. When this child first came to the class she was taken out of school, made to rest every afternoon, and kept out of doors the rest of the day. She gained a pound a week for three weeks. She was then allowed to go back to school in the morning. The rate of gain at once fell off. After three weeks more she was allowed to return to school all day, and she lost. The weight remained stationary until the middle of the summer vacation. During the fall months after school reopened especial attention was paid to this child and she began to gain, but only at the average rate. Broken line is average weight for age.

air camps are rarely of value, and the children who have been away for a few weeks for trips of this kind have been benefited little as a rule. Indeed, many have lost weight, and have reported that they have received tea, coffee, and other food which has been manifestly improper.

The influence of school is often marked. Certain children will not gain as long as they are subject to the nervous stress and confining hours of the public school. A large number begin to gain as soon as

vacation commences, and this has been true in some cases even when the child has gone to work during the summer. As a routine procedure, if a child does not gain in school, he is taken out. He is allowed to be out of doors in the morning, one or two hours rest are insisted on after the midday meal in a room with wide open windows, and he is allowed to be out the remainder of the afternoon.

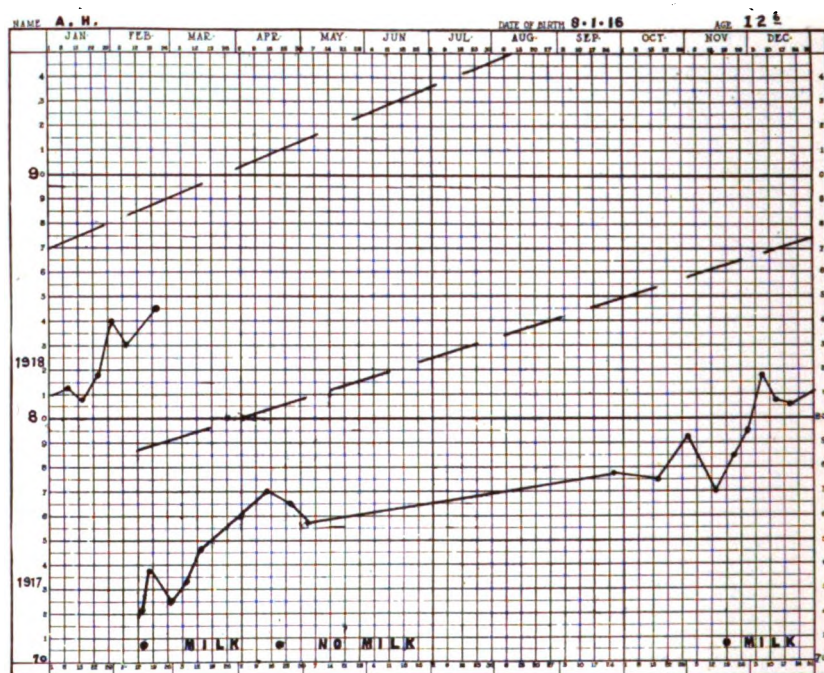


Fig. 8.—A. H., girl. On admission, weight, 72 pounds; average, $78\frac{1}{2}$; height, $57\frac{1}{2}$ inches; average, 56; average weight for height, 85 pounds. This child is over height and under weight, tall, thin, pale. Teeth, three decayed; von Pirquet, 4 plus; otherwise normal; father alcoholic; mother never attends class. Income of family, \$46 a month for six persons, or \$7.57 per person. If only 50 per cent. of this is spent for food, as economists say is proper, it means that less than 80 cents may be spent per week per person for food. It is easy to see why this child received no milk at home. When she was first admitted she was given a quart of milk a day by a charitable agency and gained 5 pounds in eight weeks. The milk was stopped, she did not attend the class and gained no weight for seven months. Milk was again furnished and she gained $7\frac{1}{2}$ pounds in three months.

In extreme cases, especially when there is marked anorexia, a complete rest cure is given. The child is kept in bed all day in a room with the windows wide open. A laxative is given each night, since constipation often results from the inactivity. The response to the rest cure is rarely delayed more than a week. The appetite invariably comes back, and a gain in weight begins. The child may then be allowed up a

few hours a day and the rest reduced to the afternoon nap. After a gain of several pounds is obtained these children are allowed to return to school in the morning, and later on for the whole day. Too often the return to school marks a cessation of the gain (Fig. 7).

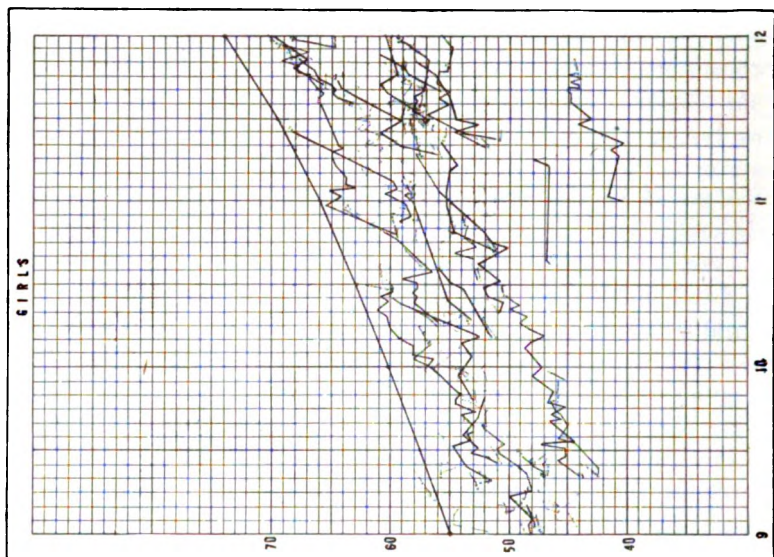
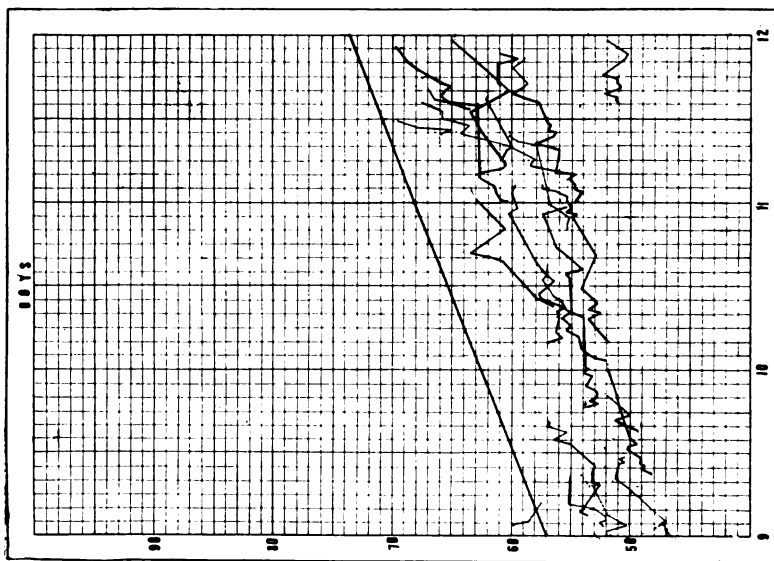
Weight Charts.—Weight charts are used for every child. These are of two types: The *individual weight chart* is printed on a stiff card the same size as the history folder. It is ruled off in pounds and half pounds, covers 25 pounds in a vertical direction, and fifty-two weeks in a horizontal. Each vertical line is dated so that the weight can be charted on the actual day of the month. This makes the charting much more rapid and simple than attempting to calculate the age of the child in years and months, weeks and days; and since we merely desire to show gains and losses it enables us to have a much larger chart and make the gains and losses relatively larger than is possible on a chart based on the child's age. If desired, the average line can be plotted so that the child can see how far below average his weight actually lies. These charts can be used for more than one year, as a rule, the line simply beginning over again at January when December is finished.

Important facts, such as tonsillectomy, acute illness, etc., may be noted to account for great variations in weight. The children learn to interpret the charts and can readily tell good from bad. There is no question that they are valuable in stimulating the child to try to gain weight. Several examples are reproduced to show the manner in which they are used (Figs. 5, 6, 7 and 8).

The second might be called the *collective charts*. These are large wall charts printed on a heavy coated cloth (size 22 by 30 inches). The weights of the entire class are plotted on these as well as the average normal weight line. Each one covers a period of three years by months, each square representing a pound in the vertical direction and a month in the horizontal. Each child's curve is plotted according to his weight and age. The girls and boys are charted separately. In cases in which the curves lie too near together, half the curves are transferred to another sheet.

Figures 9, 10 and 11 illustrate the use of the collective weight charts. In the first place, they show how much below the average weight for age the children have been. It is apparent that the children fall into two rough groups: those only moderately under weight (about 1 year or 5 to 10 pounds), and those much under weight (more than 1 year or over 10 pounds). These correspond in a general way to Groups III and IV of the Dunfermline scale.

It is evident that the younger children (and this is true for both boys and girls) are less under weight than the older. The reason for this may be that since they are younger they have had less time to fall behind. In the case of the older children the causes of the mal-



Figs. 9 and 10.—Collective weight charts of children in the Nutrition Class. Each irregular line represents the weight curve of a single child. Figures at the bottom indicate years, each square one month in a horizontal direction. Figures at the left indicate pounds, each square one pound vertically. Average weight line for age plotted on each chart.

nutrition have operated for a longer time and there is a greater weight deficit. The gain in weight has been much less at the younger ages, and it may be noted that only a few have gained at more than the average rate. This may be explained by the fact that it is more difficult to appeal to children under 9 years. They are not so much interested in trying to gain, as a rule, while the response is easier to obtain from older children. Perhaps an additional factor is that the tendency to gain weight is greater as puberty is approached, and this natural stimulus to growth exerts its force if the opportunity is given by any improvement of the diet and hygiene of the child.

In general, the weight curves which lie near the average line show a larger gain than those much below the average. This is probably because the children who are most underweight are most difficult to help. The causes of their malnutrition must be more serious and more difficult to remove than the causes which have affected the children only slightly underweight.

By means of the collective weight charts it is simple to compare with the average line the progress of the individual children and of the class as a whole. A general view of the charts gives an impression as to how the children are doing. By measuring the vertical and horizontal extent of any one of the curves, the weight gained and the time under observation are obtained. The average line may be measured for the corresponding length of time and the result compared with the first measurement. For example, a weight curve covers six and one-half months from left to right and 9 pounds from below up. The average line covers $4\frac{1}{2}$ pounds in the same length of time so that the child has gained at twice the average rate. A piece of cardboard ruled on the top to correspond to the months, and on the left to correspond to pounds makes this measurement of the curves rapid and simple.

A *photograph* is taken of every child in the class, and is pasted on the back of the weight chart. This is done very inexpensively by taking three or four children at once and cutting up the finished prints. The photographs have value in helping the physician and nurse to recall to mind any child who has been absent for a long time. They also arouse the interest of the children in the class and later photographs are useful in showing improvement. It is easy to take fairly good pictures with an inexpensive camera, by taking time exposures, and by using one of the newer high powered nitrogen lamps if necessary.

Home Records.—Sheets⁷ are used for the purpose of having the child or mother record what happens to the child each day. In many

7. This form was devised by Dr. H. L. Dowd for use in the Huddleston Memorial Class for Cardiac Children.

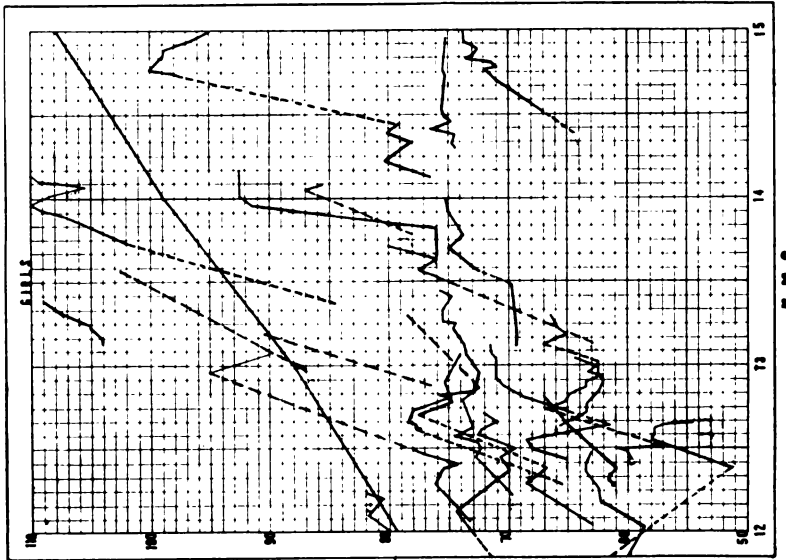


Fig. 12.—Collective weight chart of children with heart disease who have been under control. Continuous portions of each curve represent time spent at home; broken portions the time spent at Pelham Home.

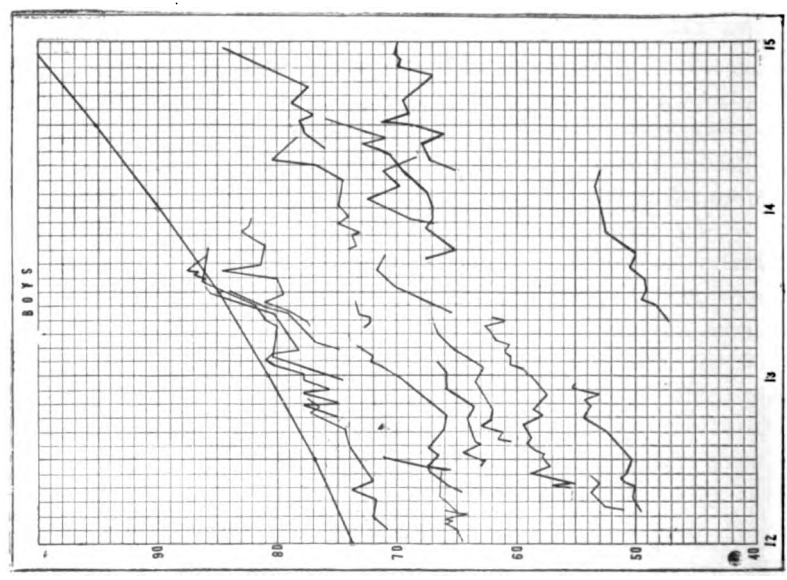


Fig. 11.—Collective weight chart of older boys in the Nutrition Class.

instances this home record has enabled us to pick out the reason for failure to gain when the verbal report had given us no clue (Fig. 13).

Large wall charts of coated cloth are used for summarizing facts of importance. These are ruled horizontally to hold fifty names and vertically into columns in which are entered all the data which are of interest. It is much quicker to get statistics from these sheets than from the individual charts, since all the facts of one kind appear in the same vertical column. Corresponding numbers make it easy to find the names on these sheets.

Milton S.
Mar 4 - 11

HOME RECORD CHART
Fill this out each week and bring to the Clinic

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
What time did you get up?	7:20	7:20	7:20	7	7:30	9	10:20
BREAKFAST	8:20	8:20	8:20	8:20	8	9	10:20
At what time?	8:20	8:20	8:20	8:20	8	9	10:20
What did you eat?	1 head 2 corn 1 apple	1 head 2 corn 1 apple	1 head 2 corn 1 apple	2 pieces head	2 pieces head	2 pieces head	2 pieces head
How much of each thing?							
At what time did the bottle move?	8:40	8:40	8:40	8:30	8:40	9:10	10:10
SCHOOL HOURS	9-12	9-12	9-12	9-12	9-12	No school	No school
DINNER	12	12	12	12	12	12	1
At what time?	12	12	12	12	12	12	1
What did you eat?	Chicken Soup head apple	Chicken Soup head apple	Chicken Soup head apple	Chicken Soup head apple	Chicken Soup head apple	Chicken Soup head apple	Chicken Soup head apple
How much of each thing?							
SCHOOL HOURS	1-3	1-3	1-3	1-3	1-3	NO	NO
DAY HOURS	None	None	None	None	None	None	None
ANY SICKNESS	None	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made
What did you do?	None	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made	2 hours watched play, made
SUPPER	6:30	6:30	6:30	6:30	6:30	6:30	6:30
At what time?	6:30	6:30	6:30	6:30	6:30	6:30	6:30
What did you eat?	2 eggs, corn head 4 pieces	2 eggs 2 glasses 1 glass 2 pieces head	2 eggs 2 glasses 1 glass 2 pieces head	2 eggs 2 glasses 1 glass 2 pieces head	2 eggs 2 glasses 1 glass 2 pieces head	2 eggs 2 glasses 1 glass 2 pieces head	2 eggs 2 glasses 1 glass 2 pieces head
How much of each thing?							
What did you eat between meals?	an apple	an apple	an apple	an apple	an apple	an apple	an apple
What time did you go to bed?	9	9:11	9	9:15	9:20	9:30	9:44
Did you sleep well?	yes	yes	yes	yes	yes	yes	yes
REMARKS							

Fig. 13.—Home record chart as filled out by the child.

Causative Factors.—Although this article deals with methods in the main, a brief summary of the causative factors which we have found may be here included.

The causes which seem to be most prominent may be divided into two main groups:

1. Malnutrition due to real disease or abnormal condition.
 - (a) Tuberculosis is the most common real pathologic condition which gives rise to malnutrition without giving marked symptoms or signs. This tuberculosis is not pulmonary, but usually in the lymph nodes in the mediastinum or elsewhere. It may be latent or active at the time the

patient comes under observation, and the malnutrition may be the only sign, aside from the positive skin reaction. The diagnosis is difficult, since the physical signs of diseased bronchial nodes are so slight as to be easily overlooked. D'Espine's sign and the roentgen ray at times are of service in clearing up the diagnosis. An irregular fever is the most suggestive sign of active tuberculosis.

(*b*). Chronic absorption from decayed teeth, diseased tonsils, chronic otitis, ozena or any other local focus of infection is quite sufficient to cause malnutrition.

(*c*). Defective nasal breathing due to enlarged adenoids or obstructed nasal passages is a common condition found among these children and must be corrected before the nutrition can be improved.

(*d*). Prematurity, small size at birth, or difficult feeding in the first year may place on a child a handicap which may not be outgrown.

(*e*). Severe or repeated gastro-intestinal attacks in the first few years, chronic indigestion especially of the intestinal type, and frequent attacks of cyclic vomiting are among the less common causes for undernutrition in older children.

(*f*). Serious illness (as typhoid or severe pertussis) or a combination of several acute infectious diseases within a few months may cause a loss of weight from which it sometimes takes years to recover.

Syphilis, diabetes, chronic nephritis, malaria, intestinal parasites and all other wasting diseases must be ruled out before a case can be considered simple malnutrition. There is also a small number of children in whom there is a change or deficiency in some of the internal secretions which is responsible for the small size. These cases are not easy to recognize when they are not of the typical varieties.

2. Malnutrition due to faulty hygiene and diet. It is important to bear in mind that bad habits of living are due to two main fundamental causes — poverty and ignorance. When the former is the main cause, it is of course more difficult to improve a child's condition. Educational efforts directed at the ignorance of the parents, when well received, offer the greatest hope of success. Bad racial habits of living may be added to the foregoing (as in Italians).

The bad habits of living include every phase of the daily life of the child. They may be briefly summarized as follows:

(*a*). Insufficient food. A very large proportion of the children of the poor receive too little to eat. A breakfast of coffee and a roll, lunch of tea or weak soup and bread, and a supper of meat and potatoes, or of a dish of macaroni, is a diet which furnishes one third to one half the necessary number of calories for proper growth. This is a sample of a day's dietary which appears again and again on our history sheets. In many cases children go to school with no breakfast,

or have no lunch at all, especially when the mother goes out to work. Even in families in which the income is adequate the food taken by the child may be insufficient in amount on account of ignorance of the parent or some whim of appetite of the child.

(b). Improper food is also commonly taken. Tea and coffee, fried food of all kinds, pies and pastries, cakes and sweets, raw fruit in excess, too much meat (twice or three times a day) are only a few of the errors in this direction.

(c). Bad habits of eating, such as eating too fast, washing down food with copious draughts of water, and eating at very irregular hours all tend to cause indigestion and to prevent the proper utilization of the food taken.

(d). Constipation or irregular bowel habit have been almost the rule among the children when they have first come to the class. It has been a rare exception to find a child whose bowels have moved regularly at the normal time, after breakfast and before school. Unless this normal habit can be established, it is practically impossible to make a child gain in weight.

(e). Insufficient sleep. Most children in the tenements sit up late and as a consequence get up late. The result is too little sleep, and too little time before school in the morning, so that the child must rush off to school without breakfast or movement of the bowels. The afternoon rest or nap is abandoned as soon as a child is old enough to struggle through the day without it, which may be as young as two years.

(f). Insufficient fresh air by day and by night. Long school hours and short days mean that no school child can be out more than an hour after school through the winter months. Windows are rarely opened at night. The crowded flat is lighted by gas, with a stove keeping the temperature of the kitchen well above 80, while the bedrooms are unheated and unaired. This makes a combination which predisposes to respiratory infections and results in general ill health.

(g). Insufficient exercise in the fresh air, or too much exercise with insufficient food and rest.

(h). Uncleanliness of body and clothing. Dirty mouths and noses have a more direct influence on the general health than dirty skins, perhaps, but there can be little question that bathing predisposes to health.

Results.—An analysis of 110 cases has been made to determine the results of the class experiment. Children have been selected who have been under observation from six to fifteen months, because it is only by taking such cases that the results can be fairly estimated. A great many children gain very rapidly in the first few weeks of their atten-

dance, but do not continue to do well for long. The shorter cases have therefore been excluded. In none of the 110 children has there been found any organic disease of importance. There are in attendance at the class a number of children who have more or less active tuberculosis (not pulmonary, but probably of the bronchial lymph nodes). These children are not included in the summary. They are allowed to attend the class because they need exactly the same attention as the malnutrition cases, and it may be said that their response to the class treatment has corresponded in general to that of the other children, except when they have had fever. They have not been transferred to the children's tuberculosis class because they have not pulmonary disease, and it is extremely undesirable to put on a child the stigma of tuberculosis unless there is some good reason for it. Under the present rules of most institutions, it is not possible to send such children to a preventorium unless there is another case of tuberculosis in the family, so the nutrition class seems to be the best place for them. There are, of course, a large number of children who have latent tuberculosis who are included in the 110 summarized, since many of them have strongly positive von Pirquet reactions.⁷

Of the 110 children, fifty-nine were girls, fifty-one boys. This whole group has gained at about one and one quarter times the expected rate for their ages. Sixty-three children (57 per cent.) have done better than the average and have gained at 1.7 times the expected rate. Of the remainder, twenty-four (22 per cent.) have gained at the average rate, and twenty-three (21 per cent.) at less than the average rate.

There is some question as to whether the children who have gained at the average rate should be included among those who have done well or among those who have done badly. There are two ways of looking at the matter. It may well be said that a child who gains at no more than the average rate is no better off at the end of the year than he was at the beginning, since he is just as much underweight. On the other hand, it is something to get any gain at all among these children, for we know that many of them have a stationary weight for months at a time, as may be seen from the weight curves of some of the children who have done badly. It is to be hoped that a start in gaining, even if only at the average rate, may be followed by a more rapid gain later on.

The best single gain was that of a boy who gained 12.5 pounds in six months, which was at five times the average rate. The worst two boys gained at only six tenths the average rate.

7. Of 152 children in which the von Pirquet was accurately observed, the reaction was positive in 82 cases, or 54 per cent.; negative in 70 cases, or 46 per cent.

The results in a class of this kind may be compared with that of a controlled group of children. The Huddleston Memorial Cardiac Class has had the privilege of sending children to the Pelham Manor Summer Home for the past year. Children with heart disease have been sent there for rest and care. Of thirty-two girls with organic heart disease who were at Pelham for an average of three and one-half months the gain was at $3\frac{1}{4}$ times the average rate. Several of them gained 15 to 18 pounds in three to four months. The lives of these girls were under careful supervision, their daily régime was properly regulated, and they had enough to eat. This shows how easy it is to obtain large gains with classes under complete control. Figure 12 shows one of the weight charts of these children and includes the girls from 12 to 15 years. The portions of the curves which are solid represent the weights while the children were at home, the broken lines are while they were at Pelham.

The class is composed of children of many races; about one third are Italians, one third Jews, one fifth Irish. They come in large part from one of the poorest sections of New York City. The average income per month for the family, divided by the number in the family, gives an estimate of the income per person per month. This income per person for the 110 children included in the summary has been \$12.40 per month. This is not an accurate measure, because children are not supposed to have as much money spent for their food as adults. It gives a rough measure of income, however, and has the advantage of simplicity. The sixty-three children who have gained at more than the average rate have had an income per person per month of \$12, or a little less than the class average, showing that it has not been entirely a question of having more money to spend. The children in Group III have averaged \$12, those in Group IV, \$13. Here again poverty does not seem to have been a factor.

Of the twenty-three children who have done least well—that is, who have gained at less than the expected rate—the following facts are significant:

The incomes of the families of 17 of the children average only \$9.50 per person per month.

The mothers of 15 children never attend the class.

The von Pirquet reaction is 2 to 4 plus in 13.

The races are, Italian 9, Irish 7, Jews 3, miscellaneous 4. This is a higher percentage of Italians and Irish and lower of Jews than the distribution in the entire class. Many of the Italian mothers speak no English, and it is to be expected that the proportion of children who have done badly would be higher in this race.

Relief.—The usual charitable agencies have been appealed to in most cases needing relief. There have been no funds at the disposal

of the class, but the Bellevue Social Service Department has been most kind in giving emergency aid when it has been needed. Small sums have also been given for milk or other food and for clothing by some of the volunteers interested in the work. This experiment has not been one in relief work primarily, but in educating the mothers and the children in matters of every day life.

The results obtained are far from ideal. It must be remembered, however, that we have been dealing with the poorest class of dispensary patients; that the first months of such work must be largely spent in obtaining equipment and devising methods; that the numbers treated are so large that the amount of individual attention given to each child has been reduced to a minimum; and that the past year has been the worst year in the history of the country as far as the rise in price of food and the disproportionate rise in wages. Under these circumstances it is remarkable that even these results have been obtained.

CONCLUSIONS

By the use of the class methods described it has been possible to make 57 per cent. of the children gain at 1.7 times the average rate for their ages, and 22 per cent. at about the average rate, or a total of 79 per cent. who have gained at or better than the average rate. Of the remaining 21 per cent., there is one or more easily ascertained reasons for the failure in every case. These results have been obtained under the most adverse circumstances.

It seems fair to conclude that the class method is of value in the treatment of undernourished children, even when they must be handled in large numbers. The establishment of such classes in all out patient departments, and perhaps in many of the schools, would be of great service to every community, not only by the good done the children treated, but also by the education of the public in matters of hygiene. Parents must be made to realize that a thin child is not a healthy child, and that he needs medical supervision.

The problem of infant mortality has been solved in large part by means of classes for teaching mothers the care and feeding of infants. If the malnutrition problem can be attacked on a large scale by similar means, there is little doubt that comparable results will be obtained.

253 West Seventy-Fifth Street.

STUDIES OF INFANT FEEDING. X.

THE DIGESTION AND ABSORPTION OF FATS. I.

CALCIUM IN ITS RELATION TO THE ABSORPTION OF FATTY ACIDS *

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AND

LOUISE A. GIBLIN, B.S.

BOSTON

INTRODUCTION

It is a fact well recognized by pediatricists that the digestion and absorption or nonabsorption of fats is probably the source of a greater part of the troubles encountered with bottle fed infants who receive cow's milk in some modification. Frequent examinations of infants' stools to detect the presence of fats and soaps, and great care taken to prevent the continued presence of an excess of soaps in the stools, are common routines in many hospitals.

Many cases of so-called "infantile atrophy" and most cases of "fat intolerance" apparently show abnormalities with respect to fat metabolism and their general condition can be improved by withholding fats to some extent. While such cases have generally been considered to show abnormalities in their metabolism of fats, a study of them soon convinced us that the trouble is one due to a faulty feeding, for any modification of cow's milk which gives a food containing the desired amounts of fat, sugar and protein does not modify or rearrange the inorganic constituents of the milk.

Cow's milk is nature's food for the offspring of the cow, contains inorganic constituents in sufficient amounts to supply the demands of the rapid growth and development of this animal and is especially rich in calcium and phosphoric acid, substances which the young of the cow use to develop rapidly growing bone tissue, but which the infant uses very sparingly. When fed to infants in the proportions found in cow's milk or modified cow's milk these substances are greatly in excess of the amounts required to supply the demands of the infant, and hence are eliminated either in the urine or feces.

In this connection it is a noteworthy fact that notwithstanding the high calcium content of cow's milk the calcium metabolism of bottle fed infants, as measured by the calcium eliminated in the urine, is

* Submitted for publication March 28, 1918.

* From the Boston Floating Hospital Laboratories, and the Pediatric Department of Harvard Medical School.

seldom greater, and often less, than that found in breast-fed infants, most of the calcium being eliminated in the feces as insoluble calcium phosphate and calcium soaps (Table 1). While this mode of eliminating the excess calcium present in cow's milk is in one way a protection to the infant, in that it prevents the calcium from entering the body fluids and tissues in organic combination, subsequently to set up a toxic condition (unpublished work from this laboratory), it may, on the other hand, bring about marked nutritional disturbances.

TABLE 1.—THE ELIMINATION OF CALCIUM, PHOSPHORIC ACID AND FAT WITH BREAST FED AND BOTTLE FED INFANTS

	Breast Fed	Bottle Fed *
Laboratory number	108	70—1
	Grams Per 24 Hours	Grams Per 24 Hours
Calcium oxid in urine	0.069	0.025
Calcium oxid in feces	0.038	1.672
Phosphoric acid [P_2O_5] in urine	0.012	0.342
Phosphoric acid [P_2O_5] in feces	Trace	0.586
Neutral fat and fatty acids in feces..... } Fatty acids as soaps in feces..... }	0.093	0.970 4.560

* Seven hundred and ninety-five c.c. of a formula containing 2 per cent. fat, 6 per cent. sugar and 1.6 per cent. protein.

The question of calcium metabolism is being given especial attention in the laboratories of this hospital. The examination of many stools from bottle-fed infants in this connection has led us to believe that although neutral fat, free fatty acids and soaps may all be found in these stools, the appearance of neutral fat and fatty acids, except in the case of diarrhea, are wholly secondary, and in most cases do not in any way indicate an impaired digestion or absorption, but rather a faulty feeding which allows an excessive amount of calcium, available for soap formation, to enter the intestines where the conditions are very favorable for the formation of insoluble calcium soaps. These soaps as they are precipitated may carry down with them by occlusion both neutral fat and free fatty acids. If the possibility of the excessive formation of insoluble calcium soaps is removed by the feeding of a decalcified milk, or one with a calcium content about equal to that found in breast milk, it has been found that infants unable to handle any fat in a modified milk can take 3 per cent. of fat in a decalcified or reconstructed milk. This point is clearly demonstrated by the figures given in Table 2.

TABLE 2.—SHOWING DECREASED AMOUNTS OF FAT AND SOAP IN INFANTS' STOOLS WHEN EXCESS
CALCIUM IS REMOVED FROM FOOD. LAB. NO. 101

Date	Dry Weight, Gm.	Total Fat, Gm.	Neutral Fat and Fatty Acid, Gm.	Fatty Acid as Soaps, Gm.	Calcium Oxid, Gm.	Phosphoric Acid, Gm.	Food	Fat Ingested, Gm.
1916								
March 12. ...	6.94	4.23	0.61	3.62	0.934	0.121	Modified milk with 2 per cent. fat.	24.0
March 13.	7.44	5.19	1.84	3.35	0.765	0.124		22.2
March 14.	4.82	2.59	1.01	1.58	0.318	0.054	Decalcified milk with 3 per cent. fat	28.5
March 15.	3.09	0.66	0.26	0.40	0.012	0.007		36.0
March 16.	2.47	0.48	0.30	0.18	0.010	0.017		36.0
March 17.	2.65	0.53	0.19	0.34	0.010	0.035		31.3

I

NATURE OF THE FATTY ACIDS IN THE SOAPS PRESENT IN THE
STOOLS FROM BOTTLE-FED INFANTS RECEIVING
MODIFIED MILK

In an attempt to determine the nature of the soaps present in infants' stools we have collected a number of the firm, characteristic soap stools usually eliminated by infants receiving modified cow's milk, such infants as are often constipated and frequently show marked distention of the bowels due to the accumulation of gas.

Technic.—One-gram portions of the dry stools were extracted with acidulated ether-alcohol mixture, the extract evaporated to dryness, dissolved in chloroform and neutralized with sodium ethylate. The chloroform was distilled off and the soaps dissolved in water and filtered to remove any neutral fat present. The fatty acids were then precipitated by the addition of hydrochloric acid, dissolved in ether, the ether distilled off and then dried in a desiccator under diminished pressure. The melting points of the fatty acids separated in this manner, together with the total fat elimination per twenty-four hours, are given in Table 3.

TABLE 3.—AMOUNTS OF FAT AND MELTING POINTS OF THE FATTY ACIDS
PRESENT AS SOAPS IN THE STOOLS FROM INFANTS RECEIVING
MODIFIED COW'S MILK

Laboratory Numbers	Percentages of Fat, Sugar and Protein in Food	Grams Fat Injected per 24 Hrs.	Grams of Fat in Stools Per 24 Hours*	Melting Points of Fatty Acids Separated from Stools
	F. S. P			
70-1	2-6-1.6	15.9	5.53	54 C.
72-1	2-6-1.6	15.9	2.02	53 C.
73-1	2-6-1.75	20.3	5.03	54 C.
74-1	2-6-2	24.3	6.47	55 C.
77-1	2-6-1.6	24.3	5.01	54 C.
79-1	2-6-1.6	28.2	1.47	54 C.
80-1	2-7-2	24.3	2.26	52 C.
81-1	2-4-6-1.9	31.3	3.99	52 C.
101-2	2-8-1.25	22.2	5.19	51 C.
104-1	2-8-1.25	24.0	3.48	52 C.
109-2	2-8-1.25	24.0	4.16	53 C.
115-1	3-2-1	39.7	5.04	52 C.
116-1	2-5-4-5-2	34.1	4.68	53 C.
117-1	2-6-1.6	20.3	5.37	52 C.
118-2	2-7-1.5	18.2	4.33	52 C.
119-1	3-5-2	34.1	8.40	51 C.
120-2	2-5-5-1.6	26.1	8.19	50 C.
121-2	2-5-5-1.6	26.1	7.21	50 C.
122-2	2-5-5-1.6	22.7	2.64	54 C.
125-2	2-7-1.5	14.2	3.13	53 C.
126-2	2-6-2	25.2	4.67	52 C.
128-2	2-5-6-2.1	30.9	4.19	53 C.
129-1	3-6-3.2	50.1	7.46	53 C.

* Neutral fat, free fatty acids and fatty acids as soaps.

The fatty acids as obtained for the determination of the melting points given in Table 3 were all united, dissolved in ether-alcohol mixture, filtered through animal charcoal and evaporated to dryness, giving 13.5 gm. The product was evidently a mixture of fatty acids for, at 49 C. it was solid; at 50 C. it was partly melted; at 52 C. it completely melted.

When dissolved in chloroform 0.3 gm. required 10.9 c.c. of tenth-normal sodium ethylate to make neutral to phenolphthalein. The average molecular weight would thus be

$$\frac{0.3}{10.9 \times 10^{-4}} = 275.2$$

The melting points given in Table 3 and the average molecular weight as found in the equation given seem to indicate that the soaps in the stools are soaps of the higher fatty acids found in butterfat, and in order to learn something of the nature of these fatty acids they were dissolved in water by adding sodium hydroxid and then precipitated as lead soaps by the addition of lead acetate, the lead soaps being then filtered, washed with water and dried. The fatty acids were then separated into four fractions in the following manner:

Fraction 1 was obtained by extracting the dried lead soaps with ether to remove the lead oleate. The ethereal solution of lead oleate was then placed in a separatory funnel with some distilled water, a few drops of nitric acid added and the lead nitrate washed out by the addition of several successive portions of water. It was found impossible to remove all the lead in this manner, so the ether was evaporated off, water added and the oleic acid converted to the sodium soap by the addition of a small amount of sodium carbonate, the soap solution thus obtained being centrifugalized and the oleic acid recovered from the clear solution by precipitating with hydrochloric acid, dissolving in ether and drying. We obtained 2.9 gm.

The lead soaps remaining after the extraction of the lead oleate were suspended in water, decomposed by the addition of a few drops of nitric acid and the free fatty acids removed by extracting with ether in a separatory funnel. The ether was distilled off, the acids dissolved in alcohol, filtered through animal charcoal and evaporated to dryness, leaving a mixture of fatty acids having a melting point of 54 C.

This product was found to contain some lead so it was dissolved in water by the addition of sodium carbonate, centrifugalized, and the fatty acids precipitated by adding nitric acid. The fatty acids were washed with several portions of water acidulated with nitric acid, then with pure water and finally dissolved in alcohol and separated into Fractions 2, 3 and 4 by crystallization.

Fraction 2 when examined under the microscope showed pure needle-like clusters of crystallized palmitic acid, and after being washed with cold alcohol and dried gave 4.5 gm. having a melting point of 62 C.

Fraction 3, when examined under the microscope, showed a preponderance of palmitic acid crystals and a few irregularly formed globules. On being dried, this fraction gave 2.2 gm. having a melting point of 56 C.

Fraction 4 was light brown in color, showed a preponderance of palmitic acid crystals and on being dried gave 2.7 gm. having a melting point of 34 C.

About 0.3 gm. of each of the fractions was dissolved in chloroform and titrated with tenth-normal sodium ethylate and the average molecular weights calculated in the manner just given. The results obtained, together with the other data relating to the fatty acid fractions separated from the infant's stools, will be found in Table 4.

We recovered 12.3 gm. of fatty acids in the four fractions. Fraction 1, containing 2.9 gm. of oleic acid, is 23.6 per cent. of the fatty acids recovered. Fractions 2, 3 and 4, containing 9.4 gm. of fatty acids, which are almost pure palmitic acid, represent 76.4 per cent. of the fatty acids recovered.

The data given in Table 4 demonstrate beyond question that a palmitate is the soap present in largest amount in the stools from

TABLE 4.—SHOWING AMOUNTS, MELTING POINTS AND AVERAGE MOLECULAR WEIGHTS OF FATTY ACID FRACTIONS SEPARATED FROM INFANTS' STOOLS

	Grams	Melting Point, C.	Grams Taken	Sodium Ethylate C.c. N/10	Average Molecular Weight
Total mixed fatty acids	13.5	50-52	0.3000	10.9	275.2
Fraction 1, oleic acid	2.9	13-15	0.3758	13.2	284.7
Fraction 2, palmitic acid	4.5	62	0.3219	12.4	259.6
Fraction 3	2.2	56	0.3625	14.0	258.9
Fraction 4	2.7	34	0.3675	13.0	282.7

Fractions 3 and 4 on being crystallized from alcohol showed a preponderance of palmitic acid crystals.

bottle-fed infants, but in order to demonstrate this more directly we have examined a number of stools from bottle-fed infants according to the following technic.

About 0.5 gm. of moist stool is placed in a small test tube, 3 drops of acetic acid and 5 c.c. of alcohol are added and the whole heated to just boiling. This gives an alcoholic solution of fatty acids which is now centrifugalized to deposit the insoluble matter and the clear liquid decanted on watch glasses and allowed to evaporate spontaneously until a marked crystallization has taken place. One drop of this mixture of liquid and crystals is now placed on a microscope slide and examined under the microscope.

In every case we found an abundance of palmitic acid crystals and could not find crystals of any other nature. It should be added that oleic acid was undoubtedly present, but as this acid is a liquid at ordinary temperatures, it would remain in solution in the last traces of the mother liquid surrounding the palmitic acid crystals.

The next point to be determined was the nature of the base which had combined with the fatty acids to form the soaps. Stools from the type of infant under consideration always show an excess of calcium over that required to form insoluble phosphates with the amounts of inorganic phosphorus present, and it seemed evident from the first that the soaps present were insoluble calcium soaps, and this suspicion was confirmed by the following procedure:

Portions of the stools were placed in Erlenmeyer flasks with 100 c.c. of water and brought to the boiling point, any sodium, potassium or ammonium soaps being thus dissolved in the water. The insoluble material was then filtered off and the fatty acids precipitated from the filtrate by the addition of a drop of hydrochloric acid. In no case was the amount of soap dissolved sufficient to produce more than a slight turbidity when the fatty acids were precipitated by the hydrochloric acid added.

It is therefore seen that the soaps present in these stools were almost wholly insoluble soaps and as calcium is the only insoluble base present in appreciable amount, it must be concluded that the insoluble soaps are calcium soaps.

II

THE SOLUBILITY OF CALCIUM SOAPS IN BILE

It will be seen from the preceding data that the proper utilization of fats by the type of infants under discussion is not a question of digestion, as has quite commonly been supposed, but rather a question of the proper absorption and assimilation of the soaps formed by the fatty acids which are produced by the digestion of fats. These soaps must be absorbed before they can be assimilated, and in order to be absorbed and pass through the intestinal wall into the body fluids they must be soluble in the intestinal juices, or, more definitely speaking, soaps must be soluble in bile in order to be absorbed and assimilated.

Cow's milk contains a large amount of calcium which is carried into the intestines with the other ingredients of the milk and is available for the formation of calcium soaps as soon as the fats are hydrolyzed by the fat-splitting ferments present in the intestinal juices. It is evident, therefore, that the absorption and assimilation of the digested fats will depend to a very great extent on the solubility in bile of the calcium soaps formed by the fatty acids produced as a result of the digestion of fats. In order to learn something of the solubilities of the calcium soaps of the fatty acids present in the fat of cow's milk, we have performed the following experiments.

A. Pure better fat was saponified by boiling under a reflux condenser with sodium ethylate. The sodium soaps thus obtained were purified and obtained in the dry condition. This mixture of soaps was very soluble in fresh ox bile, but on adding a drop of a 10 per cent. solution of calcium chlorid a heavy cloud was at once formed which settled out as a precipitate on standing. This precipitate was found to be calcium soaps.

B. Some of the mixed soaps as obtained under *A* were separated by the usual method of distillation into two fractions, the volatile fatty acids and the nonvolatile fatty acids. These two fractions were then converted into sodium soaps, the soaps being obtained in the dry condition. Both fractions were readily soluble in fresh ox bile, and on the addition of a drop of calcium chlorid the bile containing the soaps of the nonvolatile fatty acids gave a heavy precipitate, while the bile containing the soaps of the volatile fatty acids remained perfectly clear.

This difference in the solubilities of the calcium soaps formed by volatile and nonvolatile fatty acids has special significance when it is remembered that soaps of the volatile fatty acids are not found in infants' stools in more than traces except in the case of diarrheas.

In Table 5 will be found a statement of the kind and quantity of fatty acids produced by the saponification of 100 gm. of butter fat. It will be noticed that the oleic and palmitic acids together constitute over 71 per cent. of the total fatty acids thus produced, and offers some explanation for the finding previously noted that the soaps in infants' stools are soaps of oleic and palmitic acids.

TABLE 5.—MOLECULAR WEIGHTS, MELTING POINTS AND AMOUNTS OF FATTY ACIDS OBTAINED BY THE SAPONIFICATION OF 100 GM. OF BUTTERFAT¹

Name	Formula	Molecular Weights	Amounts, Gm.	Melting Points, C.
Dioxystearic acid	$C_{18}H_{36}O_4$	316	1.00	136.0
Oleic acid	$C_{18}H_{34}O_2$	282	32.50	14.0
Stearic acid	$C_{18}H_{36}O_2$	284	1.83	69.2
Palmitic acid	$C_{16}H_{32}O_2$	256	38.61	62.0
Myristic acid	$C_{14}H_{28}O_2$	228	9.89	54.0
Lauric acid	$C_{12}H_{24}O_2$	200	2.57	43.6
Capric acid	$C_{10}H_{20}O_2$	172	0.32	31.4
Caprylic acid	$C_8H_{16}O_2$	144	0.49	16.0
Caproic acid	$C_6H_{12}O_2$	116	2.09	—2.0
Butyric acid	$C_4H_8O_2$	88	5.45	—2.0

We have tried to learn something about the solubilities in bile of the calcium soaps of the nonvolatile fatty acids present in butterfat. This work is not completed as yet and the results so far obtained are rather inconclusive, but we believe calcium oleate shows a higher degree of solubility in bile at 37 C. than do the calcium soaps of stearic, palmitic or myristic acids. If this proves to be true the preponderance of the calcium soap of palmitic acid over the other soaps present in infants' stools will be readily explained.

III

THE CALCIUM CONTENT OF COW'S MILK IN ITS RELATION TO THE DIGESTION AND ABSORPTION OF FATS IN BOTTLE-FED INFANTS

So far as we know, no one before this has pointed out the important relation which exists in infant feeding between the calcium content of food and the elimination of calcium soaps in the stools. In this connection it should be understood that it is not the mere presence of calcium salts in the food which predetermines the presence of calcium soaps in the stools, for there are other factors entering into the question, such as: the forms in which the calcium is present in the food; bacterial activity within the intestines; and the amount of hydrochloric acid secreted into the stomach which may change certain forms of calcium compounds (that is, dicalcium phosphate) from an inactive to an active condition. In Table 6 will be found a statement of the different forms of calcium compounds found in cow's milk, and in Table 7 will be found data showing the influence of the different kinds of calcium salts (that is, insoluble, colloidal and soluble calcium compounds) on the elimination of calcium soaps in the stools from infants. A study of this table will show that the elimination of calcium soaps in the stools increases directly in proportion to the degree of solubility of the calcium present in the food.

1. Brown: Jour. Am. Chem. Soc., 1899, **21**, 807.

TABLE 6.—CONDITION OF CALCIUM IN COW'S MILK AND HUMAN MILK

	Grams Per 100 C.c.	
	Cow's Milk	Human Milk
Calcium as insoluble phosphate (CaHPO_4).....	0.051	None
Calcium combined with proteins.....	0.058	0.014
Calcium as soluble salts in serum (whey).....	0.045	0.021

TABLE 7.—SHOWING INFLUENCE OF KIND OF CALCIUM SALTS PRESENT IN FOOD ON THE AMOUNT OF CALCIUM SOAPS ELIMINATED IN THE STOOLS

Lab No.....	101—6	122—6	67	78—8	77—1
Age, months	6	4	4	3½	6
Kind of food.....	Synthetic	Synthetic	Synthetic	Synthetic	Milk
Formula	3-6-1.5	3-6-1.6	2-6-2	2-6-2	2-6-2
Calcium present as..	None	CaHPO_4	Calcium caseinate	Calcium caseinate and acetate	Milk salts
Grams CaO , per 24 hours	0.00	0.45	0.51	1.55	1.13
Grams P_2O_5					
Per 24 hours	0.29	0.68*	0.38	0.38	1.71
In feces per 24 hrs....					
Grams fat.....	0.53	1.36	2.14	7.90	5.01
Grams CaO	0.10	0.33	0.48	1.73	0.94
Grams P_2O_5	0.04	0.44	0.31	0.39	0.36
In urine per 24 hrs..					
Grams CaO	Trace	0.02	0.00	0.20	0.06
Grams P_2O_5	0.30	0.78	0.00	0.00	0.82

* P_2O_5 in casein..... 0.23
 P_2O_5 in CaHPO_4 0.45
 Total P_2O_5 0.68

It will be noticed from the tables that the dicalcium phosphate is practically inactive, as has been shown by us in a previous paper,² all the phosphorus fed as phosphate being recovered in the feces and the phosphorus contained within the casein being absorbed and appearing in the urine. In the case of the foods which contained calcium caseinate, and calcium caseinate plus calcium acetate, it will be seen that the urine became phosphorus free, all the phosphorus in the food being precipitated in the intestines as calcium phosphate and appearing in the feces. This question of phosphorus metabolism in relation to the calcium content of the food is one of very great importance and is being studied in this laboratory.

FAT DIGESTION AND ABSORPTION WHEN RECONSTRUCTED MILK IS FED TO INFANTS

Our investigations on infant feeding have led us to believe that many of the troubles encountered with bottle-fed infants receiving cow's milk must be attributed to the ill effects produced by the calcium in cow's milk.

2. Bowditch and Bosworth: Boston Med. and Surg. Jour., 1917, **177**, 864.

Breast milk is nature's food for the infant, and we may consider the constituents to be so balanced as to meet all the demands of growth, with a minimum of waste. Cow's milk, on the other hand, is nature's food for the offspring of the cow, and is not balanced in any respects as a food for infants, and its use as such must usually be preceded by some form of modifying which will make the quantitative relations between the fat, sugar, protein and water approximately that found in breast milk. In most, if not all, of these modified cow's milks the mineral elements present receive very little consideration, being passed over with the statement that modified cow's milk will always contain a larger percentage of ash than breast milk, and hence will furnish all the mineral elements necessary. The time has come, however, when this phase of the feeding problem can no longer be treated in this manner, and more care must be taken to see that the mineral elements are properly balanced. This adjustment must take into consideration not only the mineral elements themselves, but also their relations to the organic constituents of the food.

Metabolism studies made in this connection must be based on the fundamental assumption that the metabolism of the healthy, normal breast-fed infant shall be used as the standard for comparison, and it must be admitted that no infant fed on cow's milk or any of its modifications can present a picture of a normal metabolism. The fact that a great number of children are successfully fed on cow's milk is no justification for assuming that they present a normal metabolism, for although they may be developing and growing in a normal manner, they are doing so on an abnormal food, not the one provided for them by nature, which necessarily predetermines that an abnormal metabolism must be going on in order that they may handle this abnormal food.

The presence of large quantities of calcium soaps in the stools from bottle-fed infants receiving cow's milk is one of the striking abnormalities noticed when a comparison is made between the analyses of such stools and those from breast-fed infants. As these soaps are insoluble, they can not act as suppository in a manner similar to the sodium and potassium soaps, and as a matter of fact they often cause severe constipation, which, in our estimation, is the starting point for other complications. In studying this type of cases it soon became apparent that the removal of most of the calcium from the cow's milk presented the only possibility for the working out of a successful method of feeding them. It was at first thought that the use of sodium or potassium caseinate with whey and heavy cream would prove of some value, but the soluble calcium salts present in the whey were sufficient to cause the formation of large amounts of calcium soaps.

We have finally perfected a method for reconstructing cow's milk which permits us to remove nearly all the calcium from the original milk. This reconstructed milk possesses the advantage of a great range in its composition, as will be seen by the figures in Table 8, in which we give the composition of cow's milk, human milk and the possibilities for our reconstructed milk.

TABLE 8.—SHOWING COMPOSITION OF COW'S MILK, BREAST MILK AND RECONSTRUCTED MILK (B. F. H. FORMULA)

	Cow	Breast	Reconstructed
Fat	3.90	3.30	Any per cent. desired.
Protein	3.20	1.50	Any per cent. desired.
Sugar	4.90	6.50	Any per cent. above 2.6
Salts	0.90	0.31	(0.33)
Ash	0.70	0.20	(0.21)
Citric acid	0.24	0.11	0.17
Chlorin	0.08	0.04	0.05
Phosphorus (inorganic)	0.09	0.014	0.001 or more if desired
Potassium	0.12	0.07	0.007
Sodium	0.05	0.02	0.033
Calcium	0.14	0.03	0.009 or more if desired
Magnesium	0.012	0.003	0.008

The details for the preparation of our reconstructed milk will not be given here, for we intend to present this subject in another paper. We can say, however, that its use in all the cases so far tried has produced favorable results, and in certain cases, such as those classed as "fat intolerance" and "infantile atrophy," improvement has resulted from its use, the following case being typical.

This child always eliminated free fatty acids, neutral fats and soaps in his stools whenever a modified milk formula containing 1 per cent. or more of a fat was fed; he was always constipated and the continued ingestion of a formula containing 1 per cent. or more of fat invariably resulted in a so-called "blow up" which was always ameliorated by the withholding of fats. When our reconstructed milk was fed to this child he could digest and absorb 3 per cent. of butterfat, eliminating a stool practically free of fat, fatty acids or soaps, and his general condition improved while he received this food.

OBSERVATIONS ON THE NUTRITION AND GROWTH OF NEW-BORN INFANTS

AN ANALYSIS OF THREE HUNDRED CLINICAL CHARTS

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The medical profession is very reluctant to adopt new standards, but having been once convinced as to their correctness, they are just as loath to discard them. The result is that certain standards such as weights and measures, for example, are copied by one writer after another for years without any one, or at least very few, taking the trouble to verify their correctness. Standards which are correct in one country are often quite incorrect in another country, under different conditions.

The following observations were made from the charts in the ward for new-born of the University Hospital where, owing to the efforts of Dr. Sedgwick, chief of the Pediatric Department, and the cooperation of Dr. Litzenberg, chief of the Obstetric Clinic, all new-born infants come under the pediatric service directly after birth.

The points to be ascertained from an analysis of the charts were as follows:

The average birth weight of infants, male and female.

Average daily amounts of milk received from the mother.

Average caloric intake of babies who were gaining in weight, computed as to number of calories per kilogram of body weight.

Average initial loss in weight.

Apparent cause of the initial loss in weight.

Initial loss in weight in babies who had water in addition to the nursings, compared with that in those who had no water. (In a large series of cases every other one had water.)

Whether the initial loss in large infants was relatively greater than in smaller ones.

Average time during which the initial loss continued.

*Submitted for publication April 22, 1918.

*Read before the third annual meeting of the Middle States Pediatric Society, Dec. 10, 1917.

Average time when the babies began to regain lost weight.
 What factors seemed to determine the gain in weight.
 Had the number of stools anything to do with the failure to gain?
 What is the average daily number of stools in normal infants during the first ten days?
 Does the number of stools depend on the quantity of food received?
 What is the average gain in weight during the first ten days?
 Does the average infant regain its birth weight during the first ten days?
 The average birth weight as given by Camerer and which has been generally accepted and copied widely, is, for boys, 3,400 gm., and for girls, 3,200 gm.
 In 300 new-born infants born in the University Hospital the average weights were, boys 3,391 gm., females 3,276 gm.
 The average daily intake of breast milk was as follows:

	Days								
	2d	3d	4th	5th	6th	7th	8th	9th	10th
Our amounts, Gm.....	39	100	170	234	275	304	336	352	365
Camerer's amounts, Gm.	91	247	337	350	390	470	...	...	500

As will be noticed, our averages are much smaller. These amounts were determined by five nursings in twenty-four hours at four-hour intervals.

The caloric need of infants as computed by Heubner and Rubner is 100 to 110 calories per kilogram of body weight. This rule has been generally accepted, it being recognized and pointed out by Czerny, Keller and others that there are exceptions in which infants will gain for considerable periods on a less number of calories. Other observers including Cramer¹ and Gaus² in Europe, and Morse and Talbot³ in this country, believe that the rule of 100 calories per kilogram does not apply to babies during the first days, as they gain on less amounts. Salge points out that in cases in which infants gain apparently on a less number of calories than 100 per kilogram the milk is extremely rich in fat and the caloric deficiency is only apparent.

All of our patients who made good gains and left the hospital weighing more than the birth weight, made their gain on much less than 100 calories per kilogram of body weight.

For example, Baby 11578, weight 3,760 gm., gained 360 gm. in seven days. Calories per kilogram per day — 55, 52, 56, 67, 73, 80, 67; average, 64. Average gain per day, 51 gm.

1. Cramer: München. med. Wchnschr., 1903, **2**, 1153.

2. Gaus: Jahrb. f. Kinderh., 1902, N. S., **55**, 129.

3. Morse and Talbot: Diseases of New-Born and Infant Feeding. McMillan, 1915.

Baby 11572, weight 3,325 gm., gained 260 gm. in seven days, or an average of 37 gm. per day on an average daily quotient of 74 calories.

Baby 12505, birth weight 3,780 gm., had no apparent initial loss in weight. Received 60 gm. of milk on the second day and began to gain on the third day. This baby was complemented in order to bring up the quantity of milk to approximate 100 calories per kilogram. It was found, however, in this case, as well as in several others in which this was attempted, that the babies promptly developed diarrhea, with watery, frequent stools and the amount of milk had to be much reduced. This infant only gained 16 gm. per day on an average caloric intake of 91 per kilogram.

Baby 11565, weight 2,680 gm., began to gain on the third day after a loss of 150 gm.; got 100 gm. on the third day and began to gain on that day. It gained 180 gm. in the succeeding six days; average daily caloric intake, 53 calories per kilogram. Average daily gain, 26 gm.

Another case, Baby 10570, gained 290 gm. in five days on an average caloric intake of 43 calories per kilogram of body weight. Average daily gain, 58 gm.

This infant lost 290 gm. in the first two days, and regained the birth weight on the seventh day. None of these infants had any water. These are only a few of many similar cases.

It is apparent, therefore, that infants, at least during the first ten days, in order to gain reasonably in weight do not require anywhere near 100 calories per kilogram of body weight, that the energy quotient varies in the individual cases from 43 to 75, and that when new-born infants during the first ten days receive 100 calories per kilogram they are usually overfed. I say usually, because there are patients who will tolerate enormous quantities of food, gain steadily and rapidly for considerable periods of time without any evidence of digestive or systemic disturbance.

Regarding the caloric needs of premature infants, it is generally agreed that it is higher than for normal, full-term infants, generally conceded to be from 110 to 120 calories per kilogram.

Baby M., premature, 7 months; birth weight, 1,920 gm.; was given 85 gm. milk on the second day and increasing amounts up to 260 gm. on the sixth day, but continued to lose weight daily and lost 50 gm. on that day, on an average caloric intake of 88 calories per kilogram. The following day the amount was pushed up to 300 gm., equivalent to 100 calories per kilogram, and the baby gained 10 gm. on that day. It was kept on 300 gm. for the next twenty days and gained an average of 10 gm. per day, being discharged on the twenty-eighth day, with a weight of 2,140 gm.

Initial Loss in Weight.—According to Camerer, Schlossman and many others (Camerer's figures are generally copied) the initial loss in new-born infants occurs during the first two or three days and amounts to an average of 200 gm. "After the third day there is a

steady gain of about 30 gm. per day, and by the eighth or tenth day the baby has regained its birth weight" (Camerer).

In our series of cases the average initial loss was 240 gm. and the average time the loss continued was three days.

There have been many theories advanced as to the cause of the initial loss. These theories are so familiar that they need not be enumerated. The chief cause has generally been assumed to be the lack of food and fluid during the first days.

Shick⁴ by means of complementary feeding with mother's milk was able in nine cases to prevent the initial loss in weight. The complementary feeding was begun from three to six hours after birth and repeated every two or three hours. An amount equal to from 8 to 15 per cent. of the body weight was given irrespective of the amount received from the nursings. None of the infants suffered any inconvenience, and two actually gained in weight.

In looking over our series of charts it was noticed that the initial loss varied greatly in the individual cases and in some the loss was out of all proportion to the lack of food and fluid. For example, No. 12452, weight 3,740 gm.; got 37 gm. milk on the second day and had lost 255 gm. by the third day; while No. 12505, weight 3,930 gm., received 60 gm. milk on the second day, had no apparent loss in weight and began to gain on the third day.

The infants who are apparently normal, receive an average amount of milk, and show an unusual drop in weight at the second weighing, are frequently those who have a large amount of meconium and perhaps urine and do not pass it until after they are weighed. There is also a marked difference in the amount of vernix caseosa in different cases; so that the removal of this, coupled with the discharge of meconium and urine after weighing, would account for a considerable drop at the second weighing.

Baby 12505, who showed practically no initial loss of weight on the second day, passed a large amount of meconium at birth and had little vernix caseosa.

The continued loss in weight after the second or third day in normal infants seemed to depend on whether there was a lack of an average secretion of milk.

Concerning the effects of water in diminishing the initial loss in weight, every other baby in the series was given water up to 2 ounces after each nursing. This did not seem to affect the initial loss when an average amount of milk was secreted; the loss being as great in those who received water as in those who received none. In cases in which there was practically no milk secreted, the patients who received

4. Shick: *Ztschr. f. Kinderh.*, December, 1915.

water lost less than those who received no water. After the third day, if the milk was insufficient, water seemed to have no effect in restoring the initial loss or in preventing further loss.

The gain in weight seemed to depend on an average amount of food, varying from 43 to 74 calories per kilogram of body weight.

The initial loss in large infants, contrary to what has been generally accepted, was not relatively greater than in small ones. This agrees with Bergman's⁵ findings.

Only about one fourth of the infants regained their birth weight before leaving the hospital on the tenth day. This agrees with Bergman's findings in 1,000 cases; only about 21 per cent. had regained the birth weight by the fourteenth day, and more than half did not regain it up to the twenty-first day.

The average daily gain in weight after the third day was about 20 gm. making a total average gain of 140 gm. while in the hospital, so that three fourths of the infants left the hospital on the tenth day with an average weight of 100 gm. less than the birth weight.

Stools.—There is a great diversity of opinion among authorities as to the normal number of stools of infants during the first weeks. The number, according to different observers, varies from two to six. In our cases the stools averaged less than two per day.

In several infants who were being overfed for metabolism work, the stools became frequent and watery whenever the quantity of milk in twenty-four hours began to approximate 100 calories per kilogram. One of these cases was particularly instructive:

Baby Anderson, birth weight, 3,580 gm., was born at 7 p. m. and got 30 gm. breast milk that evening. Weights, amount of milk and loss for the first twelve days were as follows:

Day	Weight, Gm.	Milk, Gm.	Gain or Loss in Gm.
2nd.....	3,530	got 255	gain 50
3rd.....	3,470	got 290	gain 60
4th.....	3,600	got 415	gain 130
5th.....	3,670	got 480	gain 70
6th.....	3,650	got 540	loss 20
7th.....	3,750	got 750	gain 100
8th.....	3,750	got 750	no gain or loss
9th.....	3,740	got 670	loss 10
10th.....	3,730	got 775	loss 10
11th.....	3,710	got 535	loss 20
12th.....	3,710	got 550	no loss or gain—discharged

This illustrates what happens usually in overfed cases; the infants gain for a while, then, after their tolerance is exceeded, they remain stationary for a time and gradually begin to lose in weight.

These overfed infants were the only ones in which the stools were frequent and exceeded an average of two in the twenty-four hours.

5. Bergman: *Ztschr. f. Kinderh.*, March, 1916.

EVIDENCE THAT SUMMER DIARRHEA IS AN INFECTIOUS ENTERITIS *

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In a previous paper¹ I discussed the various theories which have been proposed to explain the great prevalence of gastro-enteric diseases in infants during the summer. The general conclusion in that study was that the heat theory is inadequate to explain the occurrence of diarrhea during the hot weather, although it may act as a predisposing cause. Excessively hot weather also increases the mortality of infants suffering from digestive disorders.

Three years ago the study was taken up again. The cases were studied from the practitioner's standpoint. Each case was studied carefully in regard to its history and clinical characters. The question at issue was, what kind of cases make up the class which bring about the great mortality of the summer?

First, there is the infant who has been suffering for a long period from digestive disorders, has lingered at the threshold of death, and the sudden appearance of extremely hot weather has served as the last killing factor. The sharp peak in the mortality curve is made up of a large number of these cases.

The second group of cases is made up of young children who are given new articles of diet during the summer, such as cherries, apples, strawberries, plums, green vegetables, peaches, melons, etc. These cases are rarely serious and do not add to the mortality, but increase the number of clinical cases.

A third group embraces infants suffering from acute indigestion due to overfeeding on hot days. These patients have the well known symptoms of fermental diarrhea and rapidly recover under dietetic measures. It is questionable whether these cases are much more frequent in the summer than in the winter.

A fourth group of cases is undoubtedly due to spoiled milk. These occur on very hot days when even the refrigerators and ice boxes have a temperature of 60 F. or more, and all housewives report that their milk and cream are sour. Except in infants whose nutrition is already very low, these cases are rarely serious. Vomiting is the most pronounced symptom in these cases.

Fifth, there is the dysenteric group. The infant is acutely ill, and

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1. Zahorsky, John: *AM. JOUR. DIS. CHILD.*, 1910, **6**, 289.

remains sick for one or more weeks. The disease is characterized by the passage of mucus, blood and macroscopic pus in the stool. This group is well recognized and need not be discussed at length.

Sixth, summer diarrhea.

For want of another term this name "summer diarrhea" is applied to the principal group of diarrheal diseases which occur during the summer. No doubt it is a composite group.

The characteristic symptoms of summer diarrhea are a sudden, acute onset, usually with fever and toxic symptoms, vomiting and diarrhea. The toxic symptoms, as a rule, disappear in from twenty-four to thirty-six hours (except in very young babies), the fever drops to normal, the infant feels better, but the diarrhea persists for several days; sometimes for several weeks. This persistency of the diarrhea distinguishes the disease from the ordinary fermental diarrhea from overfeeding.

The stools have only one common character, and that is they are thin and watery. The color is often green, but may be brown, yellow or gray. The watery character of the stool is easily recognized when it is freshly drawn from the rectum by a tube. After two or three days the stools become more mushy and on close inspection some mucus or mucopus will be noticed. Blood spots are occasionally observed. The acidity, as a rule, is not high except the first day of the disease, when the administration of milk has not been discontinued. I have never found the acidity in these cases as high as in ordinary fermental diarrhea (for example, after the administration of malt soup, Mellin's food, etc.).

Two years ago it occurred to me that if these cases were really infectious enteritis, some evidence of this infectious process ought to be found in the stools. From pathologic studies it is known that the principal lesions in fatal cases of summer diarrhea are swelling and ulceration of the solitary follicles. If one or more solitary follicles are infected (and it is reasonable to assume that any bacteria which enter the mucous membrane would be conveyed to the adjacent lymphoid mass), the pathologic process would be similar to that occurring in the tonsil. There would be hyperemia, swelling, and finally an extrusion of the offending micro-organisms into the intestine, accompanied by leukocytes and lymphoid cells. These leukocytes and lymphoid cells ought to be found in the stools.

I began the study of the stools two years ago, but in this report the cases are limited to those observed in private practice in St. Louis in the summer of 1917.

The technic used was as follows:

A large catheter was introduced into the rectum. In the early stage of most cases the stool readily flowed through the catheter into a

vessel. As mentioned, the stools have a variety of color, but the fluid character is marked. With a splinter of wood a small particle of this stool is mixed with 2 drops of water on a slide. It is examined under the microscope with low power.

In the vast majority of cases the field will show hundreds of leukocytes and round cells.

I have provisionally adopted the following rule in designating the amount of pus in the stool. If more than 100 cells are present, it is called pus index 100. If there is a less number of cells they are designated by approximately the number of cells counted in one field. Thus, if only 30 cells are seen, it is pus index 30. If less than 5 leukocytes are observed the pus index is zero and an inflammatory enteritis is not confirmed.

When the stools become thicker, a small mass of stool, or, if possible, a lump of mucus is mixed with the water on a slide and the cells are observed and counted as before.

Dr. J. L. Swarts, who is studying these cases with me, will report on the type of cells in a later paper.

Here I wish to emphasize that in all severe, toxic, or protracted cases of summer diarrhea in 1917, pus was demonstrable in the stools. The evidence so far goes to show that these cases are due to an infection of the solitary follicles in the upper part of the colon or the ileum. The conclusion is based on the clinical axiom that the presence of pus cells indicates an infectious process.

During the summer of 1917 we examined the stools of 85 infants suffering with diarrhea. Of these, only 12 showed macroscopic pus and blood, symptoms of dysentery. In 7 cases pus was detected only by the most careful inspection. In 53 cases pus could be found only with the microscope (See Table).

Six cases are herewith reported in detail.

CASE 1.—D. S., girl, aged 7 months. She was naturally fed for two months, when the mother's milk failed. Since then the infant has been fed on raw certified milk and thrived. At present (June 26, 1917) her food consists of 4 ounces of milk, 2 ounces of barley water, and 4 per cent. milk sugar added. She has had diarrhea for one week—eight to ten stools daily. The trouble was traced to some ice cream which had been given to the baby at a picnic. No fever has been noticed.

The baby is well nourished; skin feels dry; breathing normal; rectal temperature, 100.2 F. Physical examination otherwise negative. The stool, obtained with catheter, consists of limpid green water, the consistency of urine; acidity of this fluid, 50. Diluted with equal parts of water and a drop placed under the microscope, it shows a solid field of corpuscles. Pus index 100+.

Diagnosis, enteritis. Treatment, bismuth and rhubarb. Diet, barley water, followed after twenty-four hours by barley water and buttermilk (2 to 1).

June 29. Better; temperature 99.6 F.; stools four or five daily, thin dark, not so watery. Pus index 10. Diet, buttermilk and barley water (1 to 1) with 3 per cent. milk sugar.

SUMMARY OF CASES OBSERVED BY THE AUTHOR

No.	Age. Mos.	Sex	Date of Onset	Food	Symptoms of Onset	Fever	No. of Stools	Character of Stools	Pus Index	Febrile Period, Days	Length Illness, Days*
1	7	♀	8/ 6	Raw milk	Vomited	108	15	Watery	100	5	16
2	11	♂	6/27	Bolled milk	Diarrhea	101	5	Watery	15	6	24
3	7	♂	10/ 5	Pasteur. milk	Diarrhea	None	7	Mucous	100	..	10
4	11	♂	10/ 4	Raw milk	Diarrhea	101	9	Watery	100	2	11
5	5	♀	8/ 6	Raw milk	Diarrhea	108	20	Mucous	100	10	35
6	7	♀	9/ 1	Cond. milk	Vomiting	101	5	Watery	100	2	21
7	12	♀	7/ 5	Raw milk	Diarrhea	104	6	Slimy	100	2	5
8	14	♀	6/26	Raw milk	Vomited	None	7	Mucous	50	1	12
9	18	♀	7/12	Mixed	Diarrhea	None	6	Watery	20	..	5
10	14	♂	8/20	Mixed	Diarrhea	None	6	Watery	100	..	6
11	12	♂	8/ 6	Mixed	Diarrhea	None	5	Green	100	..	14
12	9	♂	8/ 2	Cond. milk	Diarrhea	100	4	Mucous	10	..	20
13	16	♂	9/ 5	Mixed	Diarrhea	100	8	Mucous	100	2	10
14	6	♂	9/ 6	Raw milk	Diarrhea	102	7	Mucous	100	5	14
15	1	♂	8/25	Cond. milk	Diarrhea	None	5	Green	15	..	..
16	17	♂	9/ 1	Mixed	Diarrhea	None	7	Mucous	100	..	14
17	21	♀	8/ 1	Mixed	Diarrhea	101	10	Watery	50	7	26
18	8	♀	8/ 2	Human	Diarrhea	None	5	Green	20	..	7
19	6	♂	7/ 1	Bolled milk	Diarrhea	None	7	Watery	10	..	5
20	2	♂	8/16	Raw milk	Diarrhea	None	5	Watery	50	..	13
21	5	♂	9/ 7	Bolled milk	Diarrhea	108	8	Watery	20	2	13
22	8	♂	8/23		Diarrhea	None	..	Watery	30	..	20
23	7	♂	8/ 6	Human	Fever	...	..	Loose	20	6	..
24	1	♀	6/14	Mellin's	Diarrhea	...	7	Watery	5	..	21
25	2	♂	8/ 4	Mixed	Diarrhea	None	5	Thin	5	..	3
26	13	♀	8/ 8	Mixed	Fever	100	7		10	..	3
27	15	♂	8/10	Mixed	Fever	...	15	Pus, Mucous Watery	100	5	15
28	15	♀	8/17	Mixed	Vomiting	102	6	Watery	100	2	9
29	2	♂	9/15	Mellin's Raw milk	Diarrhea	None	6	Watery	100	..	10
30	10	♀	9/20	Raw milk	Fever	102	10	Bloody	100	7	13
31	7	♂	9/ 6	Raw milk	Diarrhea	None	6	Mucous	100	..	16
32	24	♂	9/ 6	Raw milk	Diarrhea	108	5	Blood, Mucous	100	2	9
33	12	♀	8/ 5	Raw milk	Fever	101	10	Watery	100	2	9
34	24	♂	7/	Mixed	Slight fever	...	..	Blood, Mucous	100	1	7
35	25	♂	8/ 8	Mixed	Anemia	102	5	Mucous	20	10	..
36	3	♀	8/31	Bolled milk	Diarrhea	...	7	Watery	100	..	8
37	2	♀	9/ 7	Human	Colic	...	2	Mucous	5	..	..
38	2	♂	9/ 7	Raw milk	Colic	...	2	Green	5	..	..
39	3	♀	9/12	Malted milk	Diarrhea	None	..	Blood, Green	100	..	6
40	14	♀	7/24	Mixed	Vomiting and Diarrhea	100	8	Mucous	100	..	14
41	1	♀	6/15	Human	Diarrhea	100	17	Green	100	4	12
42	4	♂	8/	Raw milk	Diarrhea	101	5	Mucous	10	..	7
43	1	♀	8/12	Human	Diarrhea	...	5	Green watery	20	..	4

* All cases terminated in recovery except Cases 34 and 35, in which the patients died.

SUMMARY OF CASES OBSERVED BY THE AUTHOR—(Continued)

No.	Age, Mos.	Sex	Date of Onset	Food	Symptoms of Onset	Fever	Stools No. of	of Stools Character	Index Pus	Period, Febrile Days	Illness, Length Days*
44	5	♂	9/20	Raw milk	Diarrhea	...	6	Mucous	10	..	6
45	1	♀	8/23	Human	Diarrhea	...	7	Green	100	..	15
46	4	♂		Mixed	Diarrhea	None	5	Green	20	..	16
47	4	♂	10/ 8	Raw milk	Vomiting and Diarrhea	None	7	Watery	15	..	8
48	22	♂	8/22	Mixed	Diarrhea	103	12	Bloody, Mucous	100	2	17
49	10	♀	8/ 1	Mixed	Diarrhea	101	8	Yellow	25	2	..
50	12	♀	8/25	Mixed	Vomiting	100	20	Brown, Watery	100	1	..
51	9	♂	9/ 7	Raw milk	Diarrhea	None	10	Liquid, Green	100	..	8
52	11	♀	6/ 3	Raw milk	Diarrhea	None	8	Watery	20	..	10
53	11	♀	8/20	Mixed	Diarrhea	None	6	Mucous	100	..	5
54	12	♂	8/ 3	Mixed	Fever	100	8	Mucous	100	1	6
55	9	♂	7/10	Human	Fever	102	6	Green, Mucous	100	..	20
56	5	♀	6/ 7	Bolled milk	Diarrhea	None	5	Watery	10	..	3
57	7	♀	8/29	Raw milk	Diarrhea	101	5	Watery	50	2	7
58	7	♂	7/ 7	Raw milk	Vomiting and Fever	102	14	Mucous	50	10	12
59	3	♀	7/16	Bolled milk	Colic	None	6	Mucous	20	..	14
60	24	♂	10/ 2	Mixed	Diarrhea	None	12	Watery	100	..	30
61	14	♂	9/12	Buttermilk	Diarrhea	None	8	Watery	50	..	7
62	1	♂	10/	Human	Diarrhea	None	7	Green	100	..	7
63	15	♂	7/ 8	Raw milk	Diarrhea	99	6	Green	50	..	21
64	9	♀	8/10	Bolled milk	Diarrhea	None	8	Green	..	..	7
65	21	♂	6/16	Bolled milk	Diarrhea	None	4	Mucous	20	..	14
66	13	♀	8/25	Mixed	Diarrhea	None	3	Thin	20	..	7
67	23	♂	8/24	Mixed	Diarrhea	99	4	Thin	5	..	10
68	7	♀	6/25	Human	Diarrhea	101	8	Green	100	..	20
69	27	♀	8/ 1	Mixed	Fever	103	7	Mucous	100	..	9
70	4	♂	10/ 4	Raw milk	Diarrhea	None	5	Watery	10	..	8
71	8	♂	7/18	Bolled milk	Diarrhea	None	9	Watery	100	..	10
72	12	♀	8/23	Bolled milk	Vomiting	101	12	Watery	100	..	15
73	17	♀	7/25	Raw milk	Vomiting and Diarrhea	100	10	Watery	50	1	5
74	12	♀	7/10	Mixed	Diarrhea	None	10	Watery	100	..	7
75	7	♂	8/ 9	Cond. milk	Diarrhea	None	14	Watery	100	..	16
76	12	♀	8/25	Mixed	Diarrhea	None	11	Green, Mucous	100	..	11
77	17	♀	7/25	Mixed	Fever	None	12	Green, Blood	100	..	21
78	24	♀	8/13	Mixed	Fever	99	11	Mucous, Blood	100	..	7
79	24	♀	7/10	Mixed	Fever	104	15	Mucous	100	5	20
80	5	♂	7/16	Buttermilk	Fever	100	6	Yellow, Watery	50	1	25
81	26	♂	6/18	Mixed	Fever	101	10	Green	100	1	22
82	20	♂	8/16	Mixed	Diarrhea	None	8	Mucous	30	..	7
83	6	♂	8/10	Bolled milk	Diarrhea	102	7	Mucous	100	5	12
84	9	♀	6/10	Human	Fever	105	25	Blood, Mucous	100	3	3
85	17	♀	6/ 5	Mixed	Fever	103	20	Blood, Mucous	100	7	7

July 4. Two or three stools daily; restless; stools normal; seems hungry; weight 6,825 gm. Treatment, 6 drops paregoric twice a day. Diet, buttermilk and barley water (3 to 2), with milk sugar.

July 20. Very restless; spits up; had a chill today followed by high fever; Urine obtained in the evening full of pus corpuscles. Diagnosis, pyelitis. Temperature 105 F. Treatment, alkalies.

July 31. High, irregular fever (101 to 105 F.) for eleven days; urine almost solid with pus cells; bowels loose again. Has been on dextrinized cereal, sweet milk and cocoa during the last week. Treatment, alkalies; weight 6,356 gm.

August 4. Much better; no fever; looks very pale; weight 6,290 gm. Treatment, hexamethylenamin.

August 11. No fever for several days; urine still contains much pus; very constipated; weight 6,790 gm. Treatment, alkalies. Diet, milk and barley water sweetened with honey, bread and crackers.

September 13. Suffering with a cough and cold in the head; had high fever last night; diarrhea began again; stools watery. Pus index 100. Mucus in the stools; weight 7,230 gm. Treatment, camphor and rhubarb. Diet, barley water, to which milk should be slowly added.

September 20. Perfectly well.

CASE 2.—D. S., girl, aged 1 year; bottle fed since birth. During the previous two months she was fed on malted milk, supplemented with cereals and soup. She was put on boiled milk with flour water.

August 10. She did well for two weeks, when a diarrhea started. The father had given her ice cream. Stool thin and watery. Pus index 50. No fever. Treatment, rhubarb.

August 27. No change; nine stools in twenty-four hours; no fever; is taking one third milk and two thirds barley water; bismuth given.

August 29. Stools still very loose; brownish in color; vomited twice; slight fever during the night. Temperature 100 F. Pus index 100. Diet, barley water; bismuth; paregoric given. The baby did not return.

CASE 3.—T. H., girl, aged 2 months. The baby had been fed on raw milk, water and Mellin's food and lost in weight. When seen (August 30) had no fever; buttocks irritated; seemed hungry; no fever. Diet, baked flour and milk.

September 4. Stools twice a day; stools rather thin; gained 4 ounces; restless; same diet.

September 8. Liquid, frequent greenish stools; severe proctitis. Temperature 98.6 F.; buttocks scalded. Pus index 100 + +. Diet, casein-buttermilk.

September 10. Four stools daily; some mucus. Pus index 20. Stools mushy; no gain in weight. Add dextrimaltose.

September 15. Temperature 99.4 F. Stools yellow, mushy. Pus index 20. Weight 9 pounds 14 ounces.

September 17. Seems well; weight 9 pounds 14 ounces.

CASE 4.—R. A., girl, aged 7 months; seen first Aug. 8, 1916. The infant was naturally fed four weeks, then placed on dextrinized flour and cow's milk. She has had attacks of diarrhea all summer. Mother boils the milk when the bowels are loose and gives the milk raw when she becomes constipated. Certified milk is used. Diarrhea began again two days and fever one day before being seen.

Baby thin, but has good color; skin elastic; temperature 102.6 F.; respiration slightly hurried, not deep; stools thin, watery, no blood; microscopically full of pus. Pus index 100 +. Diagnosis, enterocolitis. Treatment, alkalies, magnesia, rhubarb. Diet, barley water for twelve hours, then buttermilk and barley water, equal parts.

August 9. Looks about the same. Temperature 101.4 F.; respiration normal; eyes bright. Tannin given. Diet, barley water and buttermilk.

August 11. Stools very loose, twelve to fifteen daily; high fever at night; temperature 102.5; weight 5,760 gm.; eyes not so bright; skin elastic. Rectal injections of buttermilk whey given twice a day. Diet, barley water mixed with dextrinized flour; two feedings of Mellin's food daily; stool still full of pus cells.

August 13. Very much better; temperature 99.1 F.; looks brighter; two stools today; vomited twice yesterday; weight 5,790 gm. Milk was tried but was vomited.

August 17. Looks well; constipated. Pus index 10. Weight 5,760 gm. Salicylic acid and rhubarb given; diet the same.

August 22. Weight 5,700 gm.; two stools daily; no pus in the stool. Diet, roasted flour, to which a little milk is to be added.

August 30. Seems well; weight 5,900 gm.; stools normal. Diet, roasted flour, milk and sugar; orange juice.

CASE 5.—V. B., girl, aged 14 months, was seen first Aug. 17, 1917. Was naturally fed a few weeks only, then given condensed milk and barley water. In October, 1916, she had an attack of diarrhea which continued more or less for three weeks. Recovered under the use of buttermilk and dextrinized flour. Had two attacks of acute respiratory infections last winter. She has been fed cereals and certified milk. Began to have frequent movements two weeks prior to being seen; was put on barley water; looseness of the bowels continued; stools green and watery. A few days later she developed cough and high fever. The temperature ranged from 103 to 105 F. the last two days.

Physical examination of the chest showed diminished breathing in the left lung, and a few fine râles.

Examination of the urine showed an enormous number of pus cells. Two days later some of the stool was drawn with a catheter and was found full of pus cells. Pus index 100. Diagnosis, pneumonia, pyelitis, enteritis.

August 25. Fever dropped to normal; left lower lobe consolidated; stools and urine still contain pus; hexamethylenamin and aromatic syrup of rhubarb given. Diet, barley water and buttermilk.

The baby slowly recovered.

CASE 6.—F. J. B., girl, aged 14 months.

June 27, 1917. Four days ago she became sick with vomiting, followed by diarrhea. She has been fed on certified milk, supplemented with cereals, broth and eggs. No other milk or ice cream has been given. She had fever the first twenty-four hours, none apparently since then; six to seven stools daily, slimy and watery in character.

Examination showed a small baby, fairly well nourished; temperature 99 F.; physical examination otherwise negative.

The stool obtained with a catheter was soft yellow, containing some fatty curds. Stool diluted one fourth contained from 30 to 40 pus cells to each field. Diagnosis, enteritis.

Diet, cereals with barley water and milk sugar. Sodium bicarbonate, magnesia, rhubarb given.

June 29. Feels much better; three stools today; temperature normal; stool firm; pus index 20. Diet, the same; bismuth subnitrate given.

July 3. One black stool daily; seems very hungry; weight 8,170 gm. Aromatic rhubarb given. Diet, $\frac{1}{2}$ pint of milk added to cereals daily.

July 12. Stools firm; good appetite; two or three stools daily; weight 8,210 gm.; temperature normal. Tincture quassiae and lactic acid given.

July 20. Stools normal; two or three stools daily, slightly sour. The infant now gets $1\frac{1}{2}$ pints of milk daily; weight 8,520 gm.

July 30. Stools good; sleeps well; one or two stools daily; feels fine; weight 8,710 gm. Diet, cereals, milk, fruit and vegetables.

The summer of 1917 was unusually cool, and no connection could be traced between atmospheric conditions and the onset of the diarrhea. Three cases ended fatally, all showed pus in the stool. Two of these cases were very severe forms of membranous dysentery and pus was passed by the teaspoonful every few minutes. In the majority of cases the infection could be traced to unboiled milk or ice cream. In three cases the source of infection could not be determined. Flies seem to have been factors in two cases. Evidence of contagion was found in three instances.

CONCLUSIONS

The summer diarrhea in St. Louis in 1917 was an inflammatory enteritis of infectious origin.

The examination of the stool for pus corpuscles is a valuable clinical aid in diagnosis.

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LYMPHATIC DISEASE IN CHILDREN SIMULATING APPENDICITIS

WITH A REPORT OF SEVEN CASES *

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In the past few weeks there have come to operation several cases of suspected appendicitis in children, but the exploration disclosed very unexpected and strikingly similar features. These were rather unusual, and in studying the records of other children who have been operated on recently in the surgical clinic, I found seven cases with the same unusual findings. In this article I shall review briefly the records of these cases, pointing out the prominent features which seem to characterize this particular syndrome.

REPORT OF CASES

CASE 1.—L. S., aged 8, was first seen in the surgical clinic Nov. 24, 1916. He had been brought to the hospital because of attacks of abdominal pain. The family history and past personal history were wholly negative. The present illness began about a year before coming to the hospital. This trouble consisted of a series of attacks of pain in the abdomen, aggravated by walking or by climbing stairs. The pain would begin each morning when the boy awoke. Examination at the hospital showed slight abdominal tenderness, not well localized. The laboratory findings were all normal. The Wassermann test was negative. The roentgenographer reported "a first degree ileal residue and a constricting zone across the cecum suggestive of adhesions and indirectly of appendicitis." A diagnosis of recurring appendicitis was made, and operation advised. At exploration, Nov. 27, 1916, the appendix was found free, long, and hypertrophic. The mesenteric and retroperitoneal lymph glands were all enlarged. The appendix and one gland were removed for microscopic examination. The pathologic report was as follows: "Appendix shows very marked lymphoid hyperplasia, no active inflammation. The swelling of the lymphoid tissue is such that the lumen is partially obliterated. The lymph gland shows also a marked lymphoid hyperplasia. This patient should be examined for enlarged glands or other evidence of lymphatic struma or hyperplasia. Our diagnosis is lymphatic struma." We were interested to learn the result of our operation, and two weeks ago I wrote to the home physician, who reported that the patient was "entirely cured and has had no further trouble," now fifteen months after operation.

CASE 2.—S. C., aged 11, was first seen Feb. 9, 1917. He also had come because of attacks of abdominal pain. The family and personal history were negative. "His attacks began in July, 1916, with sharp colicky pains in the abdomen, lasting for several minutes. He was nauseated but did not vomit.

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These pains came on several times a day and were relieved by bending over or by the application of cold. The patient had become constipated in the last year. The latest attack, which began three weeks before entering the hospital, was the most severe. This started as a generalized pain in the abdomen, which soon localized in the right side. There was vomiting but no fever. Examination showed very little except tenderness on palpation in the lower right quadrant of the abdomen." The laboratory findings were all normal; Wassermann test on the blood, negative. Operation, Feb. 14, 1917, disclosed a long free appendix, but the lymph glands in the meso-appendix and the other mesenteric nodes were all enlarged. The appendix and one gland were removed. The pathologist reported, "Lymphoid hyperplasia and chronic lymphadenitis."

CASE 3.—J. S., aged 14. This boy, the oldest of my cases, was examined July 13, 1917. He complained of "stomachache." The family history was negative, and the personal history was negative except for scarlet fever in April, 1917.

The present illness began a year before coming to the hospital. The boy gradually noticed a dull aching pain in the abdomen, which occasionally became sharp and severe. At first these pains came on at weekly intervals, but had come to be a daily occurrence. The pain came on without any apparent cause and was localized definitely in McBurney's area. Nausea was present but no vomiting. The boy would relieve the pain by doubling over. Examination showed nothing abnormal save for very definite tenderness to the right of and below the umbilicus. The laboratory tests were all normal; Wassermann negative. The roentgen ray showed a gastric and ileal residue and was diagnosed chronic appendicitis.

At operation, July 16, 1917, the appendix was found to be very long and markedly thickened. All the lymph glands in the mesentery and the retro-peritoneal nodes were enormously enlarged. The appendix and two glands were removed. Microscopic examination showed "Lymphoid hyperplasia of appendix and lymph glands."

CASE 4.—E. S., aged 12, was referred from the pediatric clinic, March 13, 1917. The family history and past personal history were negative. The patient came because of attacks of pain in the right side of the abdomen which recurred at one and two week intervals during the previous year. These attacks were all similar in nature—pain in the right lower quadrant of the abdomen, followed by nausea, vomiting and constipation. The pain did not radiate and there was no fever. The patient was sick for two or three days in each attack. Examination at the hospital was entirely negative, except for some muscle spasm and tenderness in the right lower quadrant. The laboratory findings were negative, as was the Wassermann test. The gastro-intestinal roentgen-ray examination was also negative.

The patient was operated on March 15, 1917. A long, free appendix was removed. All the mesenteric lymph glands were enlarged. No other pathology was found. The pathologic report was very terse: "Lymphoid hyperplasia."

CASE 5.—V. G., aged 7, came to the hospital because of pain in the right lower abdomen and was referred to the surgical department Dec. 10, 1917. The family history was negative. At 4 weeks of age and at 2 years, the patient had an attack of "heart trouble" but there was no evidence of intestinal trouble then. The present trouble began about a year prior to admission with pain in the right lower abdomen which lasted four or five days; no fever, no vomiting, no constipation. The child has been troubled with this pain off and on ever since. About the middle of November the girl left school because the ache was getting more and more severe.

Examination on entrance showed the posterior cervical glands slightly palpable. There was slight tenderness in the right lower abdomen, and the stomach was somewhat dilated. Blood, urine, and stomach examinations were normal; Wassermann negative. The roentgen ray showed a gastric and an ileal hypomotility. The roentgenographer said he believed that the findings justified a diagnosis of chronic appendicitis.

At operation, Dec. 11, 1917, the appendix was found to be long and hypertrophied. The distal half was free but there were some adhesions near the base. The mesenteric lymph nodes in the neighborhood, extending from the terminal ileum, appendix, and cecum were all enlarged. The appendix was removed and the pathologist reported, "No inflammation." To determine what if any effect removal of the appendix might have in changing the motility picture, a second roentgenographic examination was made fifteen days after the operation and everything was found to clear normally. The patient felt well.

CASE 6.—M. S., aged 11, entered the surgical clinic as an emergency case, Jan. 22, 1918, because of acute pain in the abdomen. The family and past personal history were negative. The present illness began in January, 1916, with an attack of pain in the right abdomen so severe that she was doubled up and could neither lie down nor stand up. The patient vomited and complained of a severe headache and constipation. The attack lasted two or three days. In the previous two years she had several minor attacks similar in nature. The last attack began three days before coming to the hospital, with severe pain in the right lower quadrant of the abdomen, headache but no vomiting.

When examined on entrance there was found marked tenderness and muscle spasm in the right abdomen; no evidence of adenopathy. The temperature was 99 F. Blood count and urine examination were normal; Wassermann negative. The patient was operated on the next day and a long, free appendix was found. The mesenteric nodes were all enlarged. The appendix and two glands were removed. The pathologic report was, "Lymphoid hyperplasia in lymph gland and appendix."

CASE 7.—S. D., aged 4 years, the youngest patient in our series, entered the surgical clinic Jan. 21, 1918, because of convulsions, epileptiform in type. The family and personal history were negative. The convulsions began the last of May, 1917. There were no prodromal signs or symptoms. One night, without warning, the boy had a generalized convulsion. The next day he was tired out. These attacks recurred at frequent intervals and were associated with severe constipation, nausea, vomiting, headaches and some abdominal pain. The patient had had osteopathic treatments (probably massage) which seemed to regulate his bowels, and just so long as he took the treatments and the bowels moved regularly, there were no attacks; but as soon as the treatments were discontinued, the constipation returned and the attacks recurred.

The physical examination, laboratory tests, and Wassermann were all negative. The gastro-intestinal roentgenogram showed gastric and jejunal hypomotility. Diagnosis, chronic appendicitis.

Jan. 27, 1918, an exploratory operation was performed. The appendix was found rather thickened but could not definitely be called pathologic. Very large lymph glands extended away from the base of the appendix and were found especially at the ileocecal junction. The lymph glands were enlarged, also, throughout the mesentery and retroperitoneal region. The appendix and several glands were removed. The pathologic report showed, "Lymphoid hyperplasia of the appendix. No inflammation. The lymph nodes showed lymphoid hyperplasia; large germ centers; exhaustion of the germ centers suggestive of lymphatic constitution." Sixteen days after the operation a second roentgenogram was taken to compare with the pre-operative plates. "The striking feature is that the hypomotility previously noted has entirely disappeared. Motility now normal."

DISCUSSION

From the foregoing digest of cases certain unusual, outstanding features impress themselves.

All these symptoms occurred in children under puberty, or who had just reached puberty. The oldest was a boy of 14 who gave evidence of rather retarded development.

In no case was there found anything in the family history to suggest an inheritance.

All presented a symptom syndrome suggestive of recurring attacks of appendicitis—not exactly a typical, textbook picture, but each presenting almost the same features and omitting others which are usually in evidence in a true infectious appendicitis. Thus, in each, the abdominal pain was the most prominent symptom, coming on in attacks lasting from a few hours to a couple of days. Each complained of nausea which in some instances led to vomiting. Constipation was a frequent complaint. Usually there was headache. In all, the pain was more or less localized in the right lower abdomen, and did not radiate.

The clinical and laboratory findings were all strikingly similar. No patient had fever; none presented a leukocytosis; urine and blood tests were in every case normal. A roentgen-ray examination was made in five of the cases and in four of the five there was a definite ileal hypomotility. The Wassermann was negative in all. In no case was any other pathology discovered than abdominal tenderness in McBurney's region. In every case the history and findings were more like appendiceal trouble than any other disease with which we were familiar, and in four instances the roentgenologist, from his standpoint, agreed with us. Yet in each and every case the pathologist reports simply and succinctly, "lymphoid hyperplasia." In two cases he amplifies this to suggest the possibility of a lymphatic constitution or lymphatism.

In trying to relate this syndrome to other known diseases, two were found to approach it:

1. Glandular fever or "Pfeiffer's disease." This is an infectious disease of children characterized by swelling and tenderness of the lymph glands, usually in the neck. In a few cases the axillary, inguinal, and sometimes the mesenteric glands are involved. The first symptoms are those of any acute infection—headache, nausea, pain in the neck and abdomen, fever to 103 F., with enlargement of the glands appearing on the second or third day. But our patients had no fever and no palpable swelling and tenderness of the superficial glands, which findings are so constant in Pfeiffer's disease. We are therefore inclined to rule out this disease.

2. Status lymphaticus. This is labeled as "a rare condition, met with chiefly in children, in which the lymph glands and lymphoid tissues throughout the body are in a state of hyperplasia. Pharyngeal thoracic and abdominal groups are most frequently affected, the cervical, axillary and inguinal glands less commonly, but may show slight enlargements." This is quite in keeping with our findings. "The lymphatic structures of the alimentary tract, the tissue of the tonsils and adenoid structures of the upper pharynx, the solitary and agminated follicles of the small and large intestines are usually much enlarged. The hyperplasia of the intestinal lymph structures may be most remarkable, the individual glands standing out like peas." This characterization of status lymphaticus is like our cases.

In no case were we able to determine thymic enlargement. One case suggests this in the early heart attacks, which were characterized by dyspnea, cyanosis and finally almost complete apnea, where death was momentarily expected for several days. Another case, in which convulsions were present, also suggests the possibility of a true lymphatism. We cannot but feel that in some way our cases are instances of a degree of lymphatic constitution which fortunately are not of an aggravated type and have not resulted in the so-called "thymic death."

The question naturally arises, is the appendix at fault? What results may we expect following its removal?

Attention was centered in the appendix because all the signs, symptoms, and clinical evidence led us to this member as the offender. Yet how it produced the symptoms cannot be said with any degree of assurance. We cannot yet explain lymphatism. Why the hyperplasia of these lymphatic structures? Is it due to a low grade, chronic infection, or is it a case of persistent intoxication? In these cases I believe that, due to the hyperplasia of the rich lymphoid tissue in the appendix, the lumen is obstructed. This was seen in two of our cases, and concretions were found at operation. We know that obstruction of an inflammatory nature, with retention of contents, can give us definite attacks of appendiceal colic. So I am inclined to interpret these symptoms as the result of a like process, but due to a definite lymphoid hyperplasia. The obstruction then gives rise to the colic and the reflex interference with the intestinal motility.

What result may we hope for? For eliminating the symptom complex which brings these patients to the hospital, it is rather encouraging. One patient has been well for fifteen months. I had hoped to be able to give definite reports on others, but I have failed to receive answers to the questionnaires which I sent out. Two patients were roentgenographed just before leaving the hospital, and from a roentgenographic

point of view, showed striking improvement. What effect removal of the appendix will have on the general glandular enlargement cannot as yet be predicted. In favorable cases I would expect atrophic changes in the thymus and lymphoid structures to take place as the child grows older; and the patient may outgrow all evidence of this affection.

This is the outcome I would like to expect for these children, appendectomy to relieve the immediate and severe manifestations of the disease, followed by ultimate disappearance of the disease through natural retrograde changes.

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